ASSOCIATION OF MATERNAL PERIODONTITIS AND RISK OF PRE ECLAMPSIA

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CERTIFICATE

This is to certify that the dissertation titled "ASSOCIATION **OF MATERNAL PERIODONTAL DISEASE AND RISK OF PRE ECLAMPSIA**" is the bonafide work done by **Dr. A. MANGAYARKARASI** between May 2009 to October 2010 during her M.D, O.G., Course at ISO – KGH, MMC Chennai.

DEAN **DIRECTOR**

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DECLARATION

I **Dr.A.Mangayarkarasi** solemnly declare that the dissertation titled "**ASSOCIATION OF MATERNAL PERIODONTAL DISEASE AND RISK OF PRE ECLAMPSIA** "has been prepared by me. This is submitted to the Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the rules and regulations for MD Examination in Obstetrics and Gynaecology. This has not been previously submitted by me for the award of any degree or diploma from any university

Place: Chennai

Date: 13.12.2010

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CONTENTS

INTRODUCTION

Hypertensive disorder complicates 5 to 10% of all pregnancies and together they form one member of the deadly triad along with haemorrhage and infection that contributes greatly to maternal mortality and morbidity rate.

Pre eclampsia is a pregnancy specific syndrome characterized by new onset hypertension, Proteinuria usually after 20 weeks gestation. It is classified into severe and non severe types and in its extreme may lead to liver and renal failure, disseminated intravascular coagulation, seizures. Pre eclampsia and eclampsia are estimated to be responsible for approximately 14% of maternal deaths per year.[1]

Despite its impact on maternal and child health, efforts to predict and prevent the disease have been disappointing. Numerous strategies have been shown to have little benefits. Because our understanding of the pathogenesis of this disease is incomplete, these preventive strategies were proposed based on pathogenetic hypothesis that did not withstand the test of time.

An increasing number of risk factors for pre eclampsia are associated with upregulation of systemic inflammation. Infection may be a risk factor capable of stimulating the cascade of inflammatory events associated with pre eclampsia. In particular the recognition of pre eclampsia as inflammatory disease has helped

researchers focus again on the potential involvement of infections in the causation of pre eclampsia.

Periodontal disease is a common oral infection, with prevalence ranging from 10-60%. A localized increase in the number and tissue invasion of certain bacteria, primarily Gram –negative organisms, causes persistent inflammation and destruction of the tissues supporting the teeth. Emerging evidence suggests that periodontal disease is also associated with systemic disease such as atherosclerotic cardiovascular disease and ischemic stroke, diabetes mellitus and erectile dysfunction. [2]

Periodontal disease may burden pregnant women systemically with endotoxin, inflammatory cytokines, and oxidative stressors at the maternal–foetal interface (Contreras et al. 2006). Thus, it may be a vascular stressor that plays a role in the development of pre-eclampsia in pregnant women. Furthermore, there is ample evidence that periodontal bacteria frequently enter the circulation causing generalized bacteremia. [3]

Infected periodontium can also be regarded as a reservoir for both microbial products and inflammatory mediators like PGE_2, interleukins (ILs) and other cytokines. Local PGE_2 and both local and systemic tumour necrosis factor-α (TNF-α) levels were increased in periodontitis [4].The proinflammatory cytokines

enter blood stream, reach maternal fetal interface, trigger or worsen maternal inflammatory response.[5]

Numerous studies suggest that periodontal disease as a source of subclinical and persistent infection, may induce systemic inflammatory responses that increase the risk of adverse pregnancy outcomes, early pregnancy loss, and preeclampsia [6]

Therefore, understanding the initiating aetiologic factor may help to design preventive and therapeutic strategies properly.

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver. It is a marker of systemic periodontal disease. CRP has been associated with adverse pregnancy outcomes, including preeclampsia, intrauterine growth restriction, and preterm delivery.[7] .

Therefore, CRP might be a plausible mediator of the association between periodontitis and adverse pregnancy outcomes.

ETIOPATHOGENESIS OF PRE ECLAMPSIA

According to National High Blood Pressure Education Working group (NHBPEP) and the American College of Obstetricians and Gynaecologists [8](ACOG) hypertension in pregnancy is defined as a diastolic blood pressure of 90mmhg or a systolic blood pressure of 140mmhg or higher after 20 weeks gestation in a woman with previously normal blood pressure. (NHBPEP.2000; ACOG 2002).This is best confirmed when evidence is present on two occasions at least 6 hours apart but within 7days.

Diastolic blood pressure is determined as the disappearance of sound (korotkoff phase v).The blood pressure level should be taken with an appropriate size cuff with the patient in an upright position after a ten minute or longer rest period. It is taken whether the patient is sitting or in the left lateral recumbent position with the arm at the level of the heart.

DIAGNOSIS OF HYPERTENSIVE DISORDERS COMPLICATING PREGNANCY

1. GESTATIONAL HYPERTENSION

BP≥140/90 mmhg, no proteinuria, BP returns to normal before 12 weeks postpartum.

2. PRE ECLAMPSIA/ ECLAMPSIA

BP≥140/90 mmhg after 20 weeks of gestation accompanied by proteinuria; eclampsia if seizures occur.

3. PRE ECLAMPSIA SUPERIMPOSED ON CHRONIC HYPERTENSION

New onset proteinuria in women with hypertension alone in early pregnancy before 20 weeks.

A sudden increase in proteinuria or blood pressure or platelets count 100,000/cu.mm in women with hypertension and proteinuria before 20 weeks gestation.

4. CHRONIC HYPERTENSION

Hypertension before pregnancy or diagnosed before 20 weeks gestation does not resolve after 12 weeks postpartum

PATHOGENESIS:

Writings describing eclampsia have been traced as far back as 2200BC (Lindheimer and colleagues, 2009) and an imposing number of mechanisms have been proposed to explain its cause. Instead of being simply “one disease”, pre eclampsia appears to be a culmination of factors that likely involve a number of

maternal, placental, fetal factors. The exact etiology of pre eclampsia remains unknown. Several theories have been proposed over the years most of which have not withstood the test of time. As Boyd stated Pre eclampsia remains "die krankheit der theorien" –**the disease of theories.** [5]

Some of the currently more accepted hypotheses include,

1. **Placental implantation with abnormal trophoblastic invasion of uterine vessels.**

   In normal implantation endovascular trophoblasts replace the vascular endothelial and muscular linings of spiral arterioles to enlarge the vessel diameter. In pre eclampsia there may be incomplete trophoblastic invasion. Diminished perfusion and a hypoxic environment eventually leads to release of placental debris that incites a systemic inflammatory response.[9]

2. **Immunological maladaptive tolerance between maternal, paternal and fetal tissues.**

   Loss of maternal immune tolerance to paternally derived placental and fetal antigens is another theory cited to account for pre eclampsia. Redman and colleagues (2009) postulated that early in pregnancy destined to be pre eclamptic, extravillous trophoblast express reduced amount of

immunosuppressive human leukocyte antigen (HLA-G) which may contribute to defective placental vascularization. [10]

3. **Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy.**

Faas(2000) proposed that endothelial cell dysfunction is due to an extreme activated state of leukocytes in maternal circulation[11]. Briefly cytokines such as tumor necrosis factor -α(TNF-α) and the interleukins (IL) may contribute to the oxidative stress associated with pre eclampsia.This is characterized by reactive oxygen species and free radicals that lead to formation of self propagating lipid peroxides.

The lipid peroxides in turn generate highly toxic radicals that injure endothelial cells, modify their nitric oxide production, and interfere with prostaglandin balance.Other consequences of oxidative stress includes production of the lipid laden macrophage foam cells seen in atherosis,activation of microvascular coagulation manifested by thrombocytopenia and increased capillary permeability manifest by edema and proteinuria.[12]

4. **Genetic factors including inherited predisposing genes as well as epigenetic influences.**

Ward and Lindheimer in 2009 [13] cited that an incident risk for pre eclampsia of 20 to 40% for daughters of pre eclamptic mothers;11 to 37 % for sisters of pre eclamptic women; and 22 to 47% in twin studies. This hereditary predisposition may likely be the result of literally hundreds of inherited genes –both maternal and paternal – that control myriad enzymatic and metabolic functions throughout every organ system.

RISK FACTORS

- Extremes of age
- Nulliparity
- Obstetric
    - Multiple gestation
    - Hydrops fetalis
    - Hydatidiform mole
- Pre existing medical disorders

- Hypertension
- Diabetic mellitus
- Renal disease
- Autoimmune disease
- Thrombophilias

- Genetic
- Family history
- Smoking
- Alcoholism

Preeclampsia is best described as a pregnancy specific syndrome that can affect virtually every organ system**.**

Minimum Criteria:

BP≥ 140/90mmhg > 20weeks of gestation

Proteinuria ≥ 300mg/24hours or ≥ 1+dipstick

INDICATORS OF SEVERITY OF PRE ECLAMPSIA

Abnormality	Non Severe	Severe
Diastolic BP	<110mg	≥110mg
Systolic BP	<160mg	≥160mg
Proteinuria	≤ 2+	≥3+
Headache	Absent	Present
Visual disturbance	Absent	Present
Upper abdominal Pain	Absent	Present
Oliguria	Absent	Present
Convulsion	Absent	Present
Sr creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Sr transaminase Elevation	Minimal	Marked
Fetal growth restriction	Absent	Obvious
pulmonary edema	Absent	Present

PROTEINURIA:

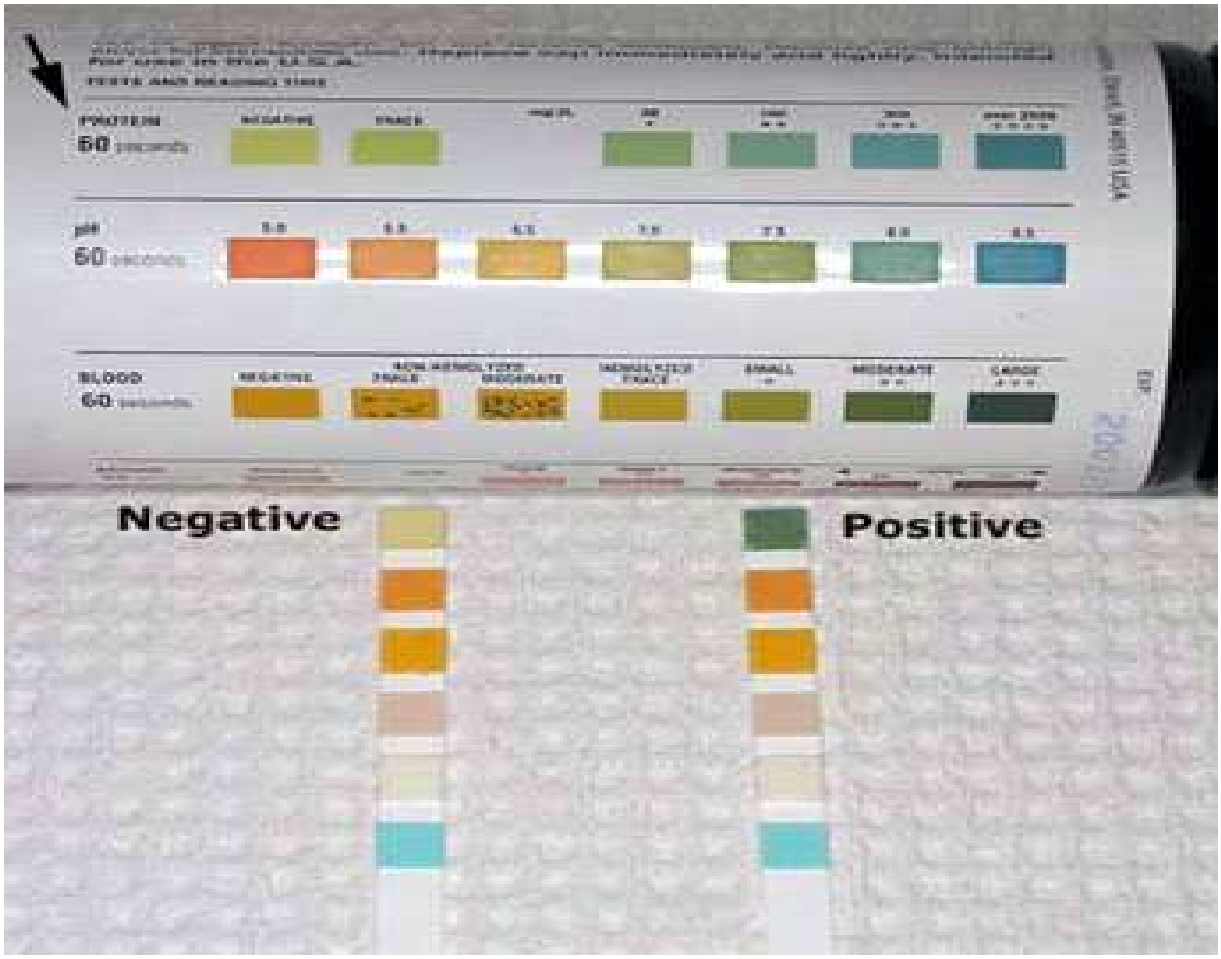
Proteinuria is defined as excretion of ≥ 0.3mg protein in a 24 hour sample which correlates with >30 mg/l or >1+ dipstick in a random sample after excluding urinary tract infection.[5]

Dipstick provides quick and simple standardized colour tests to detect protein. The strip is composed of stiff absorbent cellulose, one end of which is impregnated with the indicator “tetra-brom-phenol blue” and buffered to pH 3.

The test end of the reagent strip has to be dipped in urine and taken out immediately. Any change in colour of the test end is compared with the colour chart provided by the manufacturer.

Trace	0.1gm/L
1+	0.3gm/L
2+	1.0gm/L
3+	3.0gm/L
4+	10.0gm/L

ESTIMATION OF PROTEINURIA BY DIPSTICK



PERIODONTAL INFECTIONS

Periodontitis is an inflammation of the periodontium or one of the four tissues that support the teeth in the mouth. [14]

- The gingiva
- The cementum, or outer layer of the roots of teeth
- The alveolar bone, or the bony sockets into which the teeth are anchored
- The periodontal ligaments, which are the connective tissue fibres that connect the cementum and the gingiva to the alveolar bone.

Periodontitis is a chronic oral infection characterized by gram negative bacteria. The principal organisms implicated are

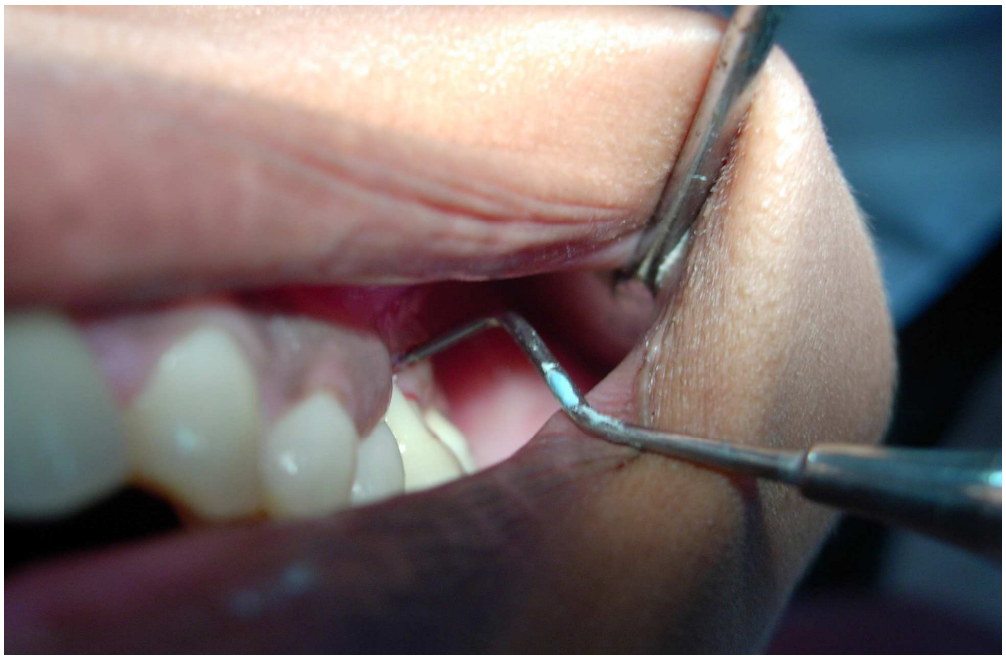
1. P. Gingivalis
2. F. nucleatum
3. E.corrodens
4. A.actinomycetumcomitants

HEALTHY PERIODONTIUM

DISEASED PERIODONTIUM

MODERATE PERIODONTITIS

SEVERE PERIODONTITIS



Symptoms of periodontitis

- Bleeding gums
- Suppuration of gums
- Halitosis and mobility of teeth

American Academy of Periodontology classification of the types of periodontal diseases [14]

Type I: Gingival Diseases: An inflammation or lesion of the gum characterized by changes of color, gingival form, position.

Type II: chronic periodontitis: An inflammation of the supporting structures of the teeth associated with plaque and calculus. It can be further classified as localized or generalized

Type III: Aggressive periodontitis: characterized by a rapid rate of periodontal disease progression in an otherwise healthy individual in the absence of large accumulations of plaque and/or calculus.

Type IV: Periodontitis as a manifestation of systemic disease

Type V: Necrotizing periodontal disease: Ulcerated and necrotic gums between teeth at the tooth margins

Type VI: Abscess of the periodontium: A localized pus forming infection of the periodontal tissue.

Type VII: Periodontitis associated with endodontic lesions: Localized deep periodontal pocket extending to the tip of the root involving pulp death.

Type VIII: Developmental or acquired deformities and condition: Gingival disease or periodontitis started by localized tooth related factors that modify or predispose to plaque accumulation.

RELATIONSHIP BETWEEN PREGNANCY AND PERIODONTAL DISEASE

Pregnancy, puberty, menstrual cycle and oral contraceptive pills all have been coupled with transient, self limiting periods of gingivitis. A common feature these conditions share is an elevation in the plasma concentration of estrogen and progesterone. Data from numerous studies states that the ovarian hormones alter the micro environment of the oral bacteria so as to promote their growth and shift in their populations.

Gingivitis in pregnancy is caused by bacterial plaque just as it is in non pregnant women. Pregnancy accentuates the gingival response to plaque and modifies the resultant clinical picture.

The aggravation of gingivitis in pregnancy has been attributed to the increased levels of progesterone, which produce [15]

1. Dilation and tortuosity of the gingival microvasculature
2. Circulatory stasis
3. Increased susceptibility to mechanical irritation
4. Leakage of fluid into perivascular tissue.

Kornman k, and Losechein 1980[16] found that during the second trimester gingivitis and ratios of bacterial anaerobes to aerobes increased.

Lapp et al [17] suggests that high level of progesterone during pregnancy causes down regulation of interleukin-6 production, rendering the gingiva less efficient at resisting the inflammatory challenges produced by the bacteria.

Gingival tissues return to their original healthy state postpartum when oestrogen and progesterone levels reach baseline values. Partial reduction in the severity of gingivitis occurs by two months postpartum and after one year the condition of gingiva is comparable to that of patients who have not been pregnant.

In some women especially in those who have a pre existing gingival pathology, this simple gingivitis can progress to periodontitis.

Preeclampsia-? Infectious etiology:

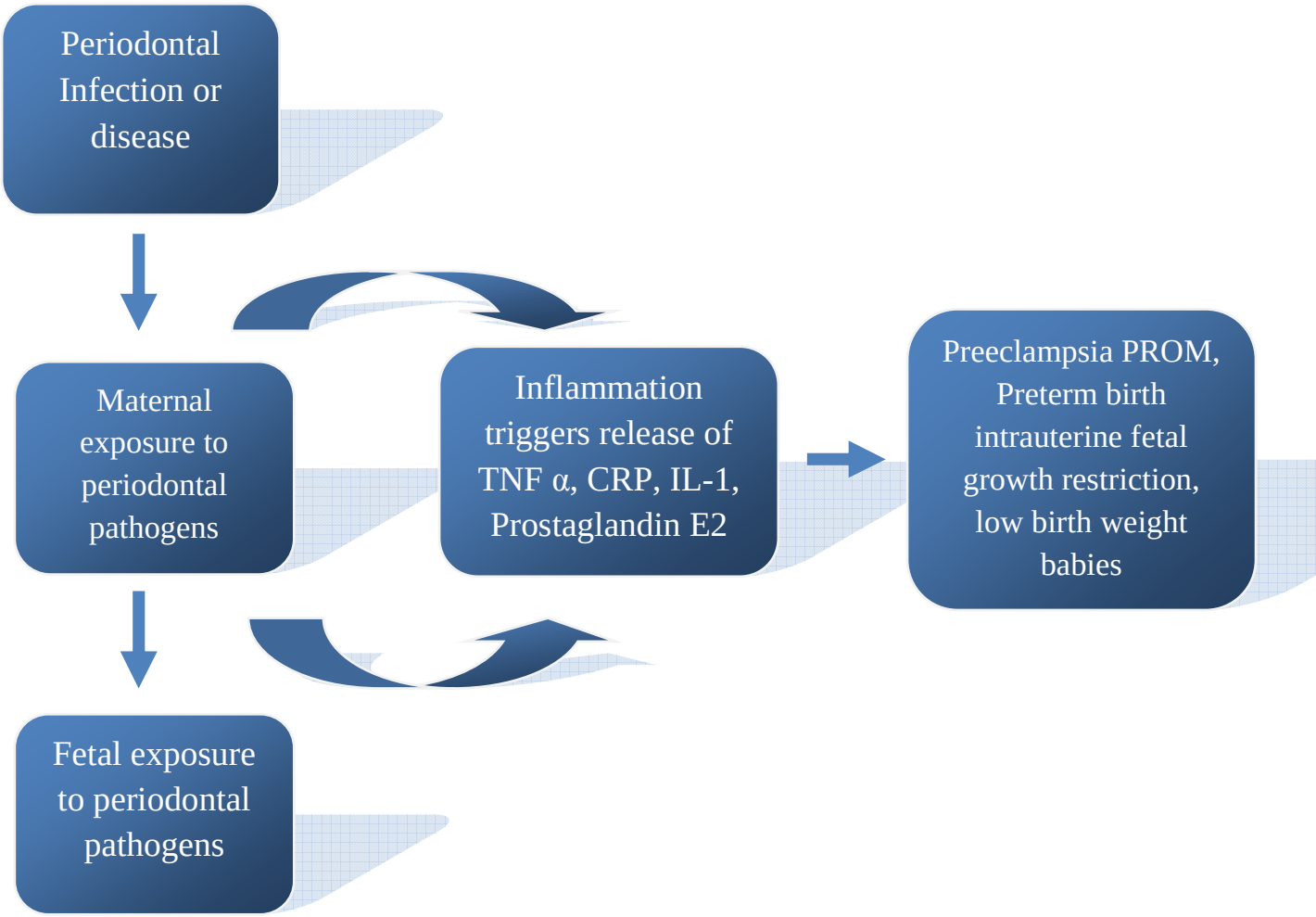
Despite active research for many years the causes of pre eclampsia remains unknown. One of the most commonly proposed mechanisms is that endothelial dysfunction associated with preeclampsia may result from a generalized maternal intravascular hyper inflammatory state.

Acute atherosis, the placental lesion of pre eclampsia shares a similar pathology, pathogenesis, and clinical setting with atherosclerosis. Recently there is increasing evidence connecting chronic infection and the formation of atherosclerosis. [18]

Contreras et al reported that periopathogenic pathogens were more prevalent in the gingival crevicular fluid of pre eclamptic patients. [19]

The chronic inflammatory nature of periodontal infection and its possible role in the initiation of atherosclerosis, together with the pathological appearance of pre eclampsia (acute atherosis) are the basics for our hypothesis for a possible role of periodontal pathogens in the development of acute atherosis, the placental lesion of pre eclampsia.

PERIODONTITIS AND PREECLAMPSIA



Periodontal disease and maternal inflammatory response mechanism

The biological mechanism to support a link between maternal periodontal disease and pre eclampsia involves micro-organisms in the oral cavity that may enter the bloodstream passively through the inflamed periodontal pocket wall or through invasive oral procedures. The maternal periodontal infection then influences fetoplacental unit in the following three ways [20,21].

1. **Action of the proinflammatory mediators**

Periodontal disease are associated with chronic gram negative anaerobic infections resulting in local and systemic elevations of proinflammatory prostaglandins, including prostaglandin E2 (PGE2) and cytokines (IL-1, IL-6, and TNF-α).

2. **The action of the periodontal reservoir of bacterial lipopolysaccharides (LPS)**

The oral micro-organisms themselves are not directly implicated in the pre eclampsia. Rather, bacterial lipopolysaccharides (LPS) (endotoxin) stimulation occurs in response to localized non-disseminating substantaneous infection with porphyromonas gingivalis (a common periodontal pathogen).

It is said that these bacterial lipopolysaccharides (LPS) can mediate the release of fever inducing IL-1 (interleukin-1), TNF-α (tumor necrotic factor α) and the hepatic release of acute phase proteins such as C-reactive protein (CRP). LPS can also target the placenta to induce the placental production of IL-1 and IL-6 resulting in inflammation of the placenta without reaching the fetal circulation.

Production of IL-1, IL-6. TNF-α, CRP and secondarily PGE2 (prostaglandin E2) modulates placental blood flow and could result in Pre eclampsia.

3. **Direct assault of micro-organism on the fetoplacental unit**

This mechanism involves translocation of periodontal pathogens to the fetoplacental unit, through the blood. Thus Periodontitis leads to a cascade of events that involve systemic maternal inflammatory responses, as well as inflammation of the fetal-placental unit resulting in abnormal pregnancy outcomes.

Periodontal disease and blood CRP levels

Periodontal disease being chronic and cyclic in nature provides an opportunity for repeated hematogenous dissemination of periodontal pathogens and direct microbial exposure of the vasculature, the liver and the placental-fetal unit among pregnant women.

The organisms can easily ingress into the peripheral circulation by way of regular chewing or any dental manipulations such as brushing or flossing. The severity of the recurrent bacteremia is said to be the principal cause of the observed association between periodontal disease and increased serum CRP levels.

Tillete and Francis in 1930 [22] were the first to discover the C Reactive protein an acute phase protein which is the primary response of the body to injury.

The C Reactive protein is so named because it forms a precipitate in a non-specific somatic reaction with the pneumococcal capsular polysaccharide in the presence of calcium ions.

In the body CRP can bind to a wide variety of substance derived from both damaged autologous cells and from micro-organisms. Complexed CRP can activate the complement system and thereby serves as a protective mechanism to the body.

Clinical measurement of CRP is valuable as a screening test for organic diseases and as an index for disease activity and response to therapy in certain inflammatory and ischemic conditions.

C - reactive protein (CRP) is synthesized by the liver in response to the inflammatory cytokines interleukin IL-6, IL-1, and TNFα tumor necrosis

factor-alpha [20]. Circulating CRP levels are a marker of systemic elevation of proinflammatory cytokines and prostaglandin. Interestingly, standard non-surgical periodontal therapy has been found to cause a decrease in serum CRP levels [23].

Evidence supporting the association between periodontitis and CRP is based mainly on studies in men and non-pregnant women. There are very few studies of periodontitis and CRP in pregnant women. CRP has been associated with adverse pregnancy outcomes, including preeclampsia, intrauterine growth restriction, and preterm delivery.

Therefore, CRP might be a plausible biological/pathologic mediator of the association between periodontitis and adverse pregnancy outcomes [24].

Treatment of Periodontitis

The therapeutic goals of periodontal therapy are [23]

1. To alter or eliminate the microbial etiology and contributing risk factor for periodontitis, thereby arresting the progression of disease and preserving the dentition in a state of health, comfort, and function with appropriate aesthetics.

2. To prevent the recurrence of periodontitis

3. Regeneration of the periodontal attachment apparatus, where indicated, may be attempted.

REVIEW OF LITERATURE

Miller in 1891 [24] published the theory of “focal infection”. On the basis of this theory, oral foci of infection were considered responsible for a number of regional and systemic diseases, such as tonsillitis, pneumonia, endocarditis and septicemia. However, the lack of scientific evidence condemned this theory to dormancy.

It was 100 years later, in the early 1990s that **Collins and colleagues** [21] hypothesized that oral infection, such as periodontitis, could act as a source of bacteria and inflammatory mediators that could disseminate systemically to the feto-placental unit via the blood circulation and induce pregnancy complications.

In a series of landmark animal studies in which pregnant hamsters were injected with the periodontal pathogen *Porphyromonas gingivalis*, Collins and colleagues [25] found that infection led to smaller fetuses (approximately 20 percent reduction in weight) and to an increase of inflammatory mediators (TNF α and PGE2) at the site of infection and in the amniotic fluid.

In subsequent experiments, in which periodontal disease was induced in pregnant hamsters, the investigators found similar results in terms of fetal growth. These were the first proof-of-principle experiments to suggest a possible association of periodontal disease with adverse pregnancy outcomes.

Three separate lines of evidence currently relate oral infection to pregnancy outcome:

1. Microbiological studies,

2. Case control studies,

3. Prospective longitudinal studies.

The first line of evidence to support a relationship between periodontitis and Pre-eclampsia is found in several **microbiological studies** of amniotic fluid, maternal and fetal cord serum, and gingival crevicular fluids (GCF).

Dr.Orit Oeltinger barak et al in 2005[26] reported findings of a one to one matched case control study (N=15) that evaluated the association between periodontitis and preeclampsia supported by immunological assessment of gingival crevicular fluid sample. Pre eclamptic group had higher probing depth and clinical attachment level compared with controls, (2.98 vs. 2.11 and 3.33 vs. 2.30 respectively). Gingival crevicular fluid prostaglandin E2 *(PGE_2),* tumor necrosis

factor *(TNF) - α,* and interleukin *(IL)-1 β* levels were also significantly higher in the pre eclamptic group.

A.Contreras et al in 2006[19] conducted a case control study to determine the effect of periodontitis and the subgingival microbial composition on preeclampsia. A total of 83 out of 130 preeclamptic women (63.8%) and 89 out of 243 controls (36.6%) had chronic periodontitis (OR: 3.0; 95% confidence interval (CI): 1.91 to 4.87; $p<0.001$) Prophyromonas gingivalis and Tannerella forsythensis, and the green complex microorganism Eikenella corrodens were more prevalent in the preeclamptic group than in controls ($p<0.01$)

Shlomi Barak et al in 2007[27] conducted a study to explore the possibility of translocation of periopathogenic bacteria into the placental tissue of women with preeclampsia. Samples were taken from 16 placentas obtained from caesarean section. Eight of the 16(50%) placenta specimens were positive compared to only two of 14(14.3%) sample from controls. Bacterial counts were significantly higher in the preeclampsia group for all periopathogenic bacteria examined ($P\leq0.0055$).This suggests the possible contribution of periopathogenic bacteria to the pathogenesis of pre eclampsia.

Each of the above studies suggests that periodontal infection is a source of microbial products causing an inflammatory response that affects the pregnancy

outcome. The studies also suggest that maternal periodontal infections, resulting in blood borne microorganisms that can translocate to the fetus, provide a systemic challenge to the fetus and induce an immunological response.

The second line of evidence comes from examining **case control studies**.

Canacki V et al in 2004 [28] carried out an matched case control study on 41 pre eclamptic and 41 normotensive pregnant women to investigate the association between periodontitis and pre eclampsia .Results showed that pre eclamptic women patients were 3.47(95%CI=1.07-11.95) times more likely to have periodontal disease.

Cota et al in 2006 [29] conducted a case control study comprising of 588 antenatal women to determine the association of maternal periodontitis and risk of pre eclampsia and found a statistically significant association between the two. (P=0.001 OR=1.88; 95%CI=1.1 to 3.0).

Kunnen et al 2007[30] conducted a case control study to investigate the correlation between maternal periodontitis and early onset pre eclampsia in antenatal women with gestational age less than 34 weeks. Severe periodontal disease was found in 14 of 17(82%) pre eclamptic women and 13 of the 35(37%)

women in the control group. There was significant correlation between early onset pre eclampsia and severe periodontal disease.

Fernanda mafro siqueira et al in 2008[31] conducted a case control study on 1206 Brazilian women divided into a control group(1042 non pre eclamptic) and a case group(164 pre eclamptic).Further 125 pre eclamptic women were matched to non pre eclamptic women randomly selected from the control group. After controlling for confounders, maternal periodontitis remained associated with preeclampsia (OR = 1.52; 95%, CI: 1.01 – 2.29; P=0.045) emphasizing the importance of periodontal care in prenatal programs.

The third line of evidence comes from **prospective studies,**

Dr. Michael S. Rumo et al in 2002[32] conducted a cohort study with 775 healthy pregnant women who had oral examinations and C-Reactive Protein (CRP) level measured at enrollment (<26 weeks gestation) and found women with periodontal disease and CRP $\geq 75^{th}$ percentile were at increased risk for pre eclampsia (adjusted RR5.8, 1.2 – 26.9) Compared to women without periodontal disease and either CRP $<75^{th}$ or $\geq 75^{th}$ percentile

Boggess KA et al [33] conducted a large prospective study with a cohort of 1115 pregnant women to determine the association of maternal periodontal disease with

development of pre eclampsia.Women were at higher risk for pre eclampsia if they had severe periodontal disease at delivery (OR=2.4.95%CI=1.1-5.3) or if they had periodontal disease progression during delivery (OR=2.1, 95%CI=1.0-4.4).

Amanda L. Horton et al in 2010[34] conducted a prospective study to determine the relationship among maternal periodontal disease, maternal oxidative stress, and the development of preeclampsia. They analyzed maternal blood for 8- isoprostane concentrations using enzyme linked immunosorbent assay and women with an 8 – isoprostane concentration $\geq 75^{th}$ percentile (38.2% versus 24.4%, p=0.07, OR: 1.91; 95% confidence interval (CI: 0.94 to 3.90) were at increased risk for developing preeclampsia.

Canaki V et al in 2007[35] conducted a study on 59 pregnancy women (20 mild pre- eclampsia, 18 severe pre eclampsia, 21 healthy pregnant women) to evaluate the possible link between the severity of periodontal disease and pre eclampsia and to correlate this link to clinical periodontal parameters and IL–1, TNF α, PGE_2 levels in both gingival crevicular fluid and serum.

After adjusting for the confounding factors, severe pre eclamptic women were 3.78 times more likely to present severe periodontal disease than normotensive pregnant women. IL–1, TNF α, PGE_2 levels in both serum and GCF were also significantly higher in the pre eclamptic groups than normotensive.

Luis O. Rustveld et al [36] conducted a systematic review in which sixteen of the 32 studies were selected for inclusion in the meta-analysis. These studies showed any infection (bacterial or viral) was associated with a twofold higher risk of preeclampsia. This association may provide a potential explanation for pre-eclampsia related inflammation (combined results for the 16 studies yielded an OR of 2.1 (95% CI 1.6 – 2.7).

Agustin condo – Agudelo et al in 2008[37] in a systematic review conducted on 49 observational studies examined the relationship between maternal infection and preeclampsia. The risk of pre eclampsia was increased in pregnant women with urinary tract infection (pooled odds ratio: 1.57; 95% CI: 1.45 – 1.70) and periodontal diseases (pooled odds ratio: 1.76; 95% CI: 1.43 – 2.18).

Periodontitis and C Reactive Protein

Tilette and France in 1930[22] were the first person to discover the C Reactive protein which is an acute phase protein produced by the body in response to injury.

M.B Pepys in 1981[22] proposed that an elevated serum concentration of CRP is an evidence of active tissue damaging processes and measurement of levels forms a screening test for organic diseases and inflammatory states. Increased CRP levels

were also a very early and sensitive response to different forms of microbial infections.

Ebersole et al in 1977 [38]compared the levels of both CRP and haptoglobulin in the serum of adult with periodontitis and in normal subjects using ELISA and found that both were elevated in the sera of adults with periodontitis. Statistically significant decrease in the values occurred after the treatment of periodontitis.

Noack et al in 2001 [39] examined the levels of CRP in patients with periodontitis and correlated it to the severity of periodontal disease and to periodontal micro flora. Results obtained showed that the extent of increase in CRP levels in patients depends on the severity of the disease after adjusting for age, body mass index and smoking.

The sub gingival plaque samples were then examined for the presence of bacteria known to cause periodontitis by immnuoflourescence microscopy. Presence of periodontal pathogens was positively associated with elevated CRP levels.

In 2006 Waranuch Pitiphat et al [40] conducted a cohort study, where they measured plasma CRP in 35 subjects with periodontitis (i.e., at least one site with ≥3mm of alveolar bone loss) and a random sample of 66 periodontally healthy

subjects matched on age and race/ethnicity. The mean CRP level was 65% higher (95% confidence interval: -2%, 180%; P=0.06) in women with periodontitis (2.46 ± 0.52 mg/l) than in controls (1.49 ± 0.22 mg/l), after adjusting for factors related to CRP levels, including age, race/ethnicity, pre-pregnancy body mass index, alcohol intake, education, income, and gestational age at blood collection.

J Herrera et al in 2007[41] investigated the effect of the severity of periodontal diseases, subgingival microbial composition and serum hs-c-reactive protein levels in preeclampsia women. He found periodontal infection with E Corrodens in all women (n-167) was associated with higher levels of hs-CRP (median 6.34 mg/dl) compared with subjects not infected with the bacteria (n -231 median 5.32 mg/dl) ($p<0.05$) .

Recently **Amanda et al in 2008** [42] conducted a study in African American pregnant women and concluded that moderate/severe periodontal diseases were significantly associated with elevated CRP levels (adjusted OR: 4.0; 95% confidence interval [CI]: 1.2 to 8.5).

All the above studies suggest that periodontitis may increase CRP levels in pregnancy. CRP could potentially mediate the association of periodontitis with pre eclampsia and other adverse pregnancy outcomes.

AIM OF STUDY

1) To identify the association between maternal periodontitis, maternal systemic inflammation and preeclampsia.

2) To investigate whether C - reactive protein is the possible mediator of the association between periodontitis and pre eclampsia.

MATERIALS AND METHODS

Study Population

The study is a prospective cohort study conducted from May 2009 – October 2010 among antenatal primi booked at Institute of social obstetrics and Govt. Kasturba Gandhi Hospital. Over this period, eligible healthy women with a singleton pregnancy were enrolled at <20 weeks gestation and followed till delivery for the development of pre eclampsia. Demographic information, health behavior and medical history data were obtained by patient interview and questionnaire at the first visit. Periodontal examinations were performed at enrollment and within 48 hours of delivery to determine the presence of

periodontal disease or periodontal disease progression. Maternal blood was collected at enrollment for estimation of C-reactive protein.

Gestational age was calculated by the date of the last menstrual period and was confirmed by a first or second trimester ultrasound examination. Details on the course of the labour, delivery and new born were abstracted from the medical record. During the period of study a total 200 antenatal women were included in the study. A written consent was obtained before their enrollment.

A detailed general examination and a meticulous local examination were performed.

INCLUSION CRITERIA

- Primi gravida between 18 to 35 years
- Women with singleton live Pregnancy

EXCLUSION CRITERIA

- Multiple gestation
- Chronic hypertension
- Diabetes
- Renal disease

- Heart disease
- Infection requiring antibiotic
- Obesity
- Current use of corticosteroids
- Presence of fetal congenital anomalies

The patients were subjected to a speculum examination to note the presence of any abnormal discharge. A drop of potassium Hydroxide was added to the secretion and the development of a fishy odour was taken as a positive test for Bacterial vaginosis. These patients were excluded from the study.

Urine was collected in a sterile container and sent to the microbiology lab where culture was done. Those with Urinary tract infection were also excluded from the study.

Pre eclampsia categorized as 2 episodes of blood pressure >140/90 mmhg and atleast 1+proteinuria in urine sample.

Maternal serum assayed for C-REACTIVE PROTEIN and stratified .

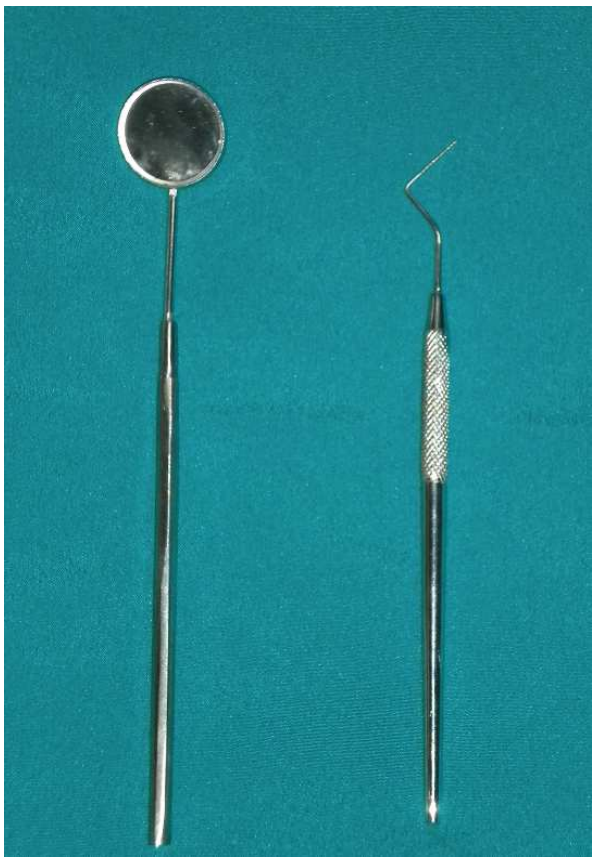
Periodontal Examination

Study participants underwent an intra-oral examination by a qualified periodontologist at enrollment and within 72 hours postpartum. The examination was carried out using a mouth mirror and William's graduated periodontal probe.

Periodontal Evaluation The probing depth and the clinical attachment loss (CAL) were the parameters that were measured.

MOUTH MIRROR & WILLIAMS GRADUATED PERIODONTAL PROBE

(with mm markings)



DETERMINATION OF PROBING DEPTH USING

WILLIAMS PERIODONTAL PROBE

Probing Depth

The distance in mm from the cemento-enamel junction to pocket base was defined as probing depth. At least 6 areas of each tooth (buccal-mesial, mid-buccal, buccal-distal, lingual-mesial, mid-lingual and lingual-distal) was examined using the periodontal probe. The highest score in mm for any tooth was recorded for probing depth.

Clinical Attachment Loss (CAL)

Attachment loss is a more accurate measure of disease severity than probing depth and is defined as the distance in mm between the cemento-enamel junction and the base of the periodontal pocket. CAL was first calculated for each tooth separately. The mean CAL value was then computed.

Periodontitis was classified as localized or generalized depending on whether <4 or ≥ 4 sites showed a probing depth of > 3 mm and CAL >1 mm.

Severity of periodontitis was classified as follows (AAP 1999):

- Periodontal health was defined as CAL<1 mm
- Mild periodontitis-CAL in the range of 1.1 – 2.9 mm
- Moderate periodontitis-CAL in the range of 3-5 mm
- Severe periodontitis-CAL>5 mm

In our study we have grouped patients with Periodontitis into two categories namely localized and generalized which is similar to the study conducted by Nabet C et al (2010)[43].

Biochemical investigations

5ml of blood was drawn from every subject for routine investigations and also for estimation of C – Reactive protein (CRP) levels.

Estimation of C – Reactive Protein by Nephelometry

Principle

Polystyrene particles coated with monoclonal antibodies specific to human CRP are aggregated when mixed with samples containing CRP. These aggregates scatter a beam of light passed though the sample. The intensity of the scattered light is proportional to the concentration of the relevant protein in the sample. The result is evaluated by the comparison with a standard of known concentration. The assigned value of CRP in CN Rheumatology standard SL is standardized against the interaction reference preparation BCR-CRM 470.

Composition

Cardiophase hsCRP reagent consists of a suspension of polystyrene particles with monoclonal antibodies to CRP.

Armamentarium

- BN System
- Cardiophase hsCRP reagent
- Five vials containing 5ml each of three vials.
- N Rheumatology standard SL
- N/T Rheumatology controls SL/1 and SL/2
- Apolipoprotein
- N supplementary reagent/precipitation
- N Diluent

Procedure

1. Allow reagents and samples to equilibrate to room temperature before use on the instrument.

2. On the instrument, samples should run at approximately the same ambient temperature (Maximum 3° deviation) as the measurements used for recording the reference curve.

Assay Protocols

The assay protocols, for serum as well as plasma, are given in the instruction manual and software of the instrument. All steps are performed automatically by the system.

Establishment of Reference Curves

Reference curves are generated by multi-point calibration. Serial dilutions of N Rheumatology standard SL are automatically prepared by the instrument using N Diluent. The standard dilutions are to be used within four hours. The reference curve is valid for four weeks and can be used beyond this period of time, as long as controls with corresponding SL/1 and SL/2 or Apolipoprotein Control Serum CHD are reproduced within their respective confidence interval. If a different lot of reagent is used, a new reference curve must be generated. The exact measuring range depends upon the concentration of the protein in which lot of N Rheumatology Standard SL.

Assay of specimens

Samples are automatically diluted 1:400 (CRPI) or 1:30 in the Cardiophase hsCRP assay protocol (CRP2) with N Diluent. The Diluent samples must be used within four hours. If the results obtained are outside the measuring range, the assay can be repeated using a higher or lower (only in the CRP1 assay protocol) dilution of the sample.

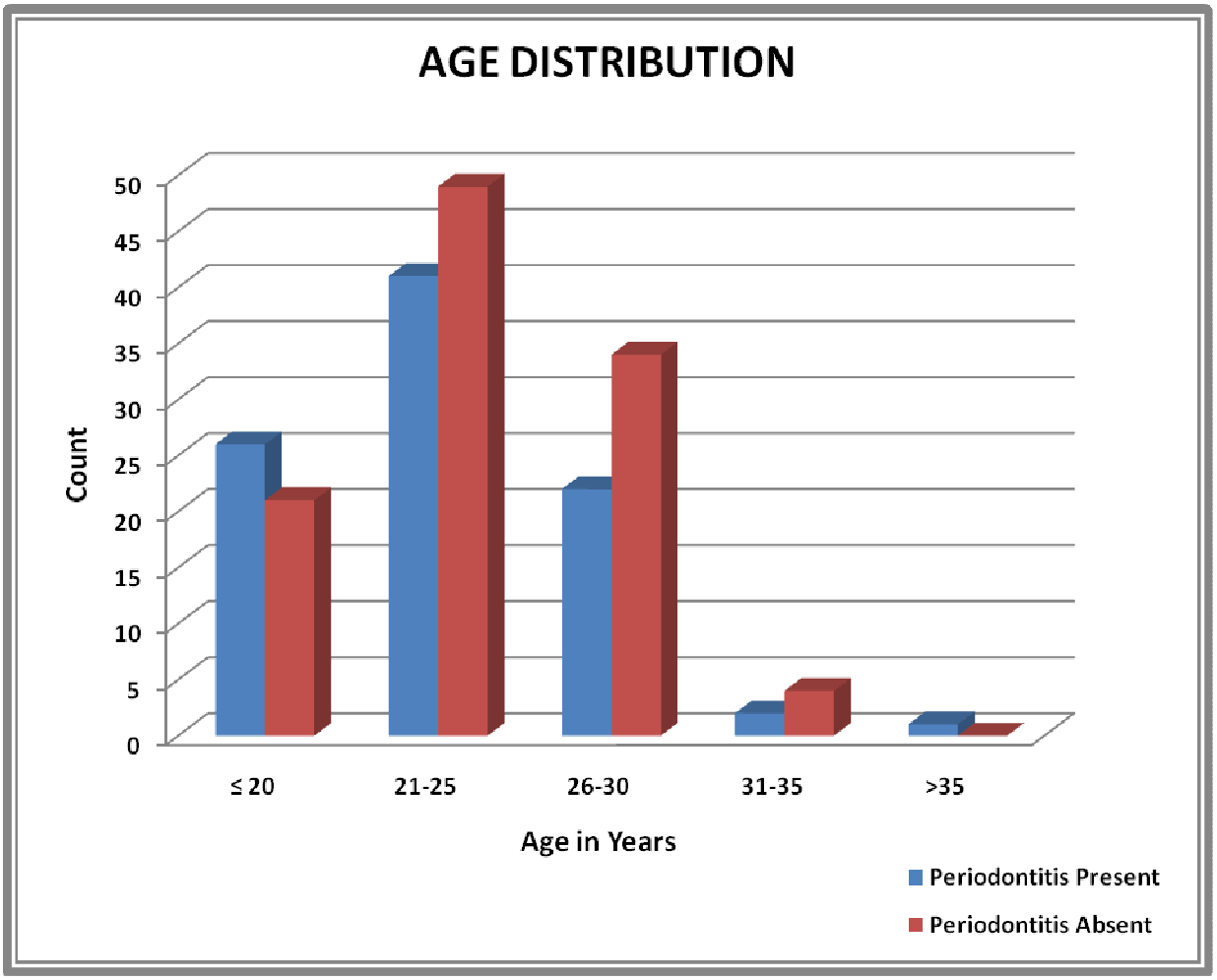
Results

The results are evaluated automatically by the analyzer and are represented in mg/L or in a unit selected by the instrument.

INSTRUMENT USED FOR CRP ESTIMATION

KIT FOR CRP ESTIMATION

RESULTS


AGE DISTRIBUTION
Count
50
45
40
35
30
25
20
15
10
5
0
≤ 20
21-25
26-30
31-35
>35
Age in Years
Periodontitis Present
Periodontitis Absent

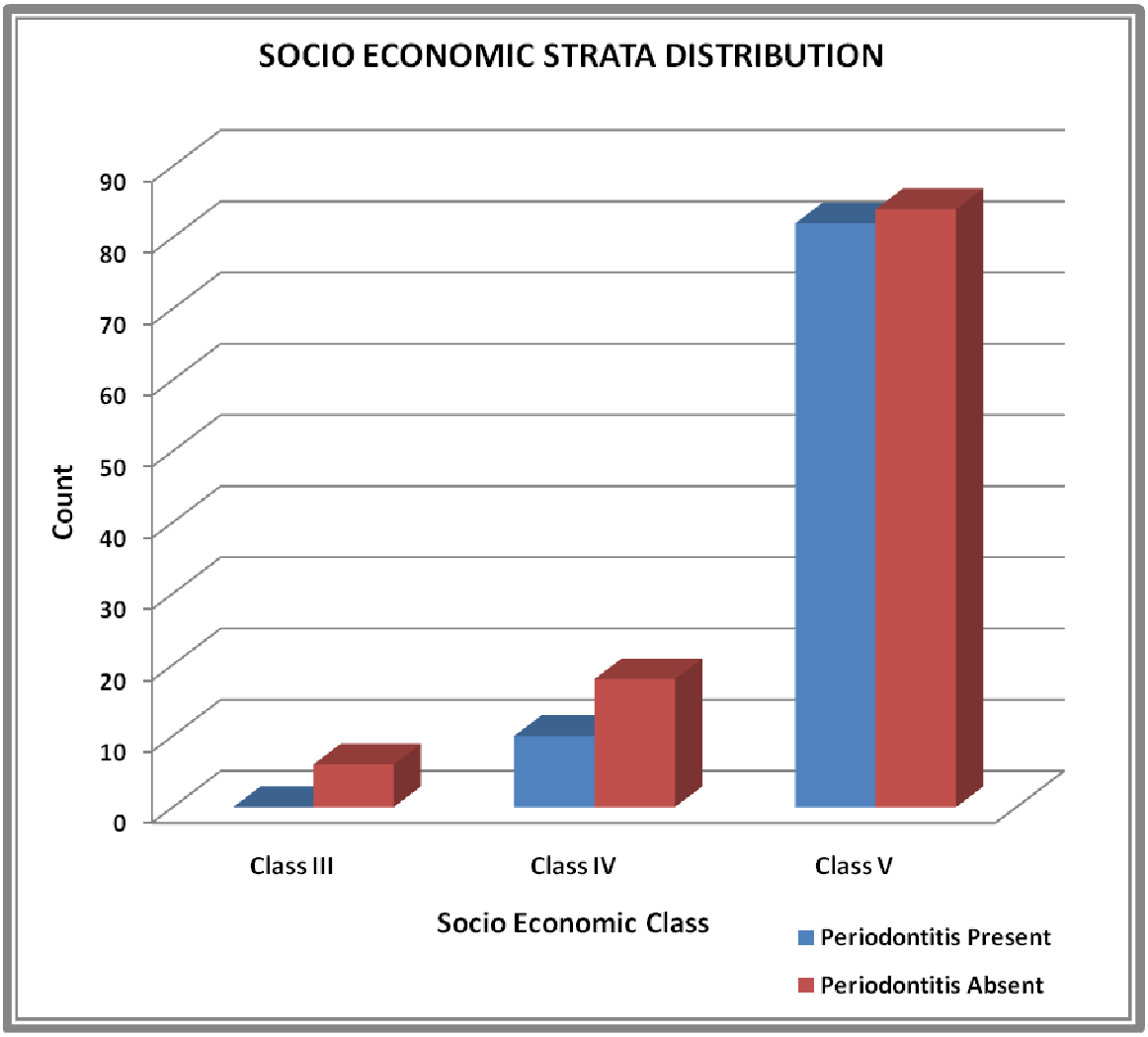
AGE DISTRIBUTION

(Table 1)

Sr. NO	Age in Years	Periodontitis Present		Periodontitis Absent	
		Number	Percentage	Number	Percentage
1	≤ 20	26	28.26%	21	19.44%
2	21-25	41	44.57%	49	45.37%
3	26-30	22	23.91%	34	31.48%
4	31-35	2	2.17%	4	3.70%
5	>35	1	1.09%	-	-

P value >0.05 → Not Significant

The average child bearing age in both groups was 23 years.


SOCIO ECONOMIC STRATA DISTRIBUTION
Count
90
80
70
60
50
40
30
20
10
0
Class III
Class IV
Class V
Socio Economic Class
Periodontitis Present
Periodontitis Absent

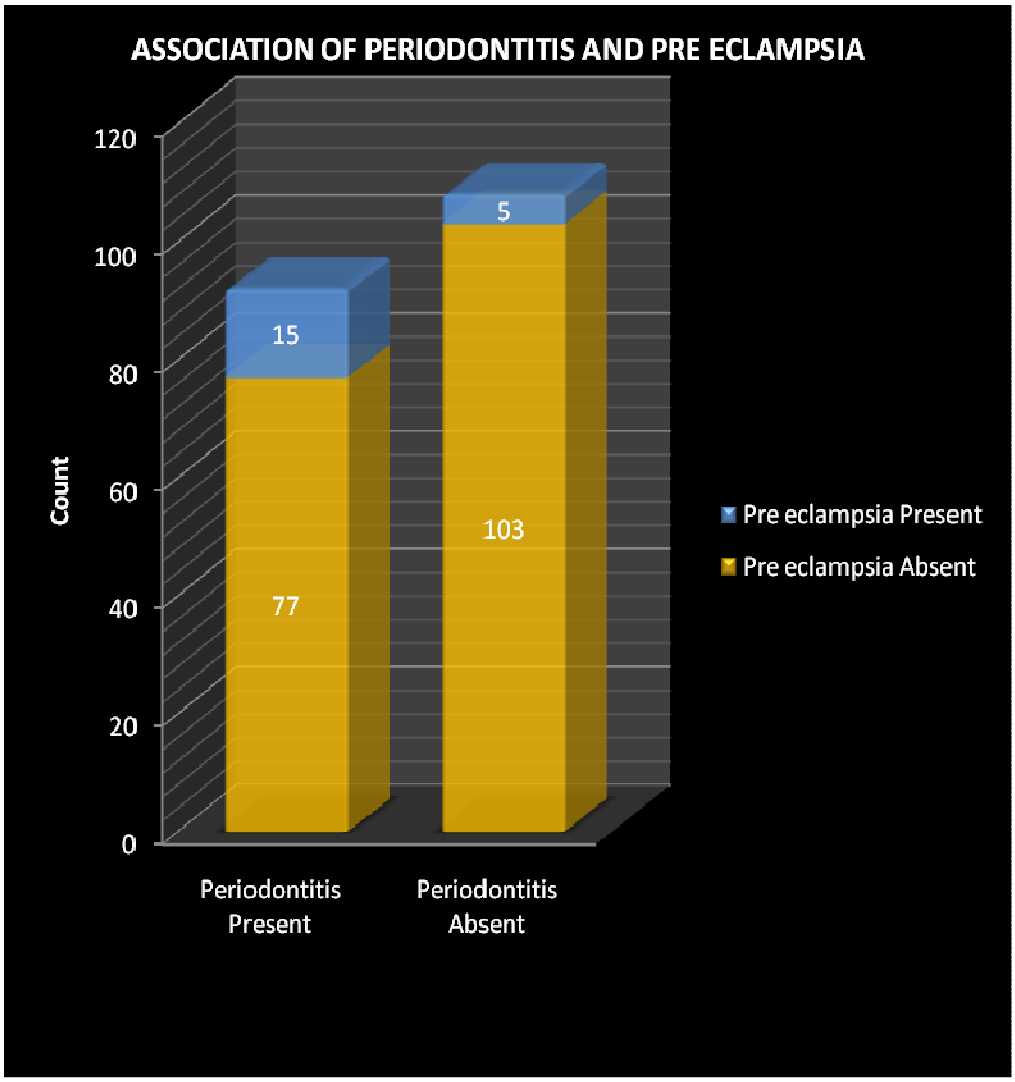
SOCIO ECONOMIC STRATA DISTRIBUTION

(Table 2)

Sr No	Socio Economic Group	Periodontitis Present		Periodontitis Absent	
		Number	Percentage	Number	Percentage
1	Class III	0	0	6	5.50%
2	Class IV	10	10.86%	18	16.67%
3	Class V	82	89.13%	84	77.78%

P value >0.05 → Not Significant

Both groups have similar socio economic stratum.


ASSOCIATION OF PERIODONTITIS AND PRE ECLAMPSIA
120
100
80
60
40
20
0
Count
15
77
5
103
Periodontitis Present
Periodontitis Absent
Pre eclampsia Present
Pre eclampsia Absent

ASSOCIATION BETWEEN PERIODONTITIS & PRE ECLAMPSIA

(Table 3)

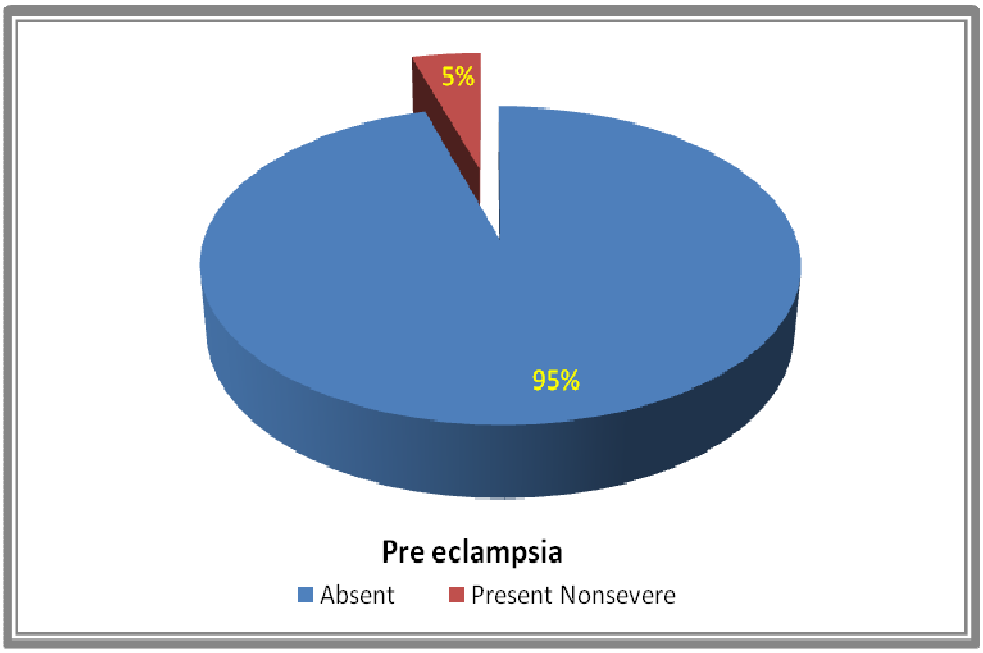
Sr No	Periodontitis	Pre eclampsia Present		Pre eclampsia Absent		Total
		Number	Percentage	Number	Percentage	
1	Present	15	16.30%	77	83.70%	**92**
2	Absent	5	4.63%	103	95.37%	**108**
	Total	**20**		**180**		**200**

Chisquare value: 6.28

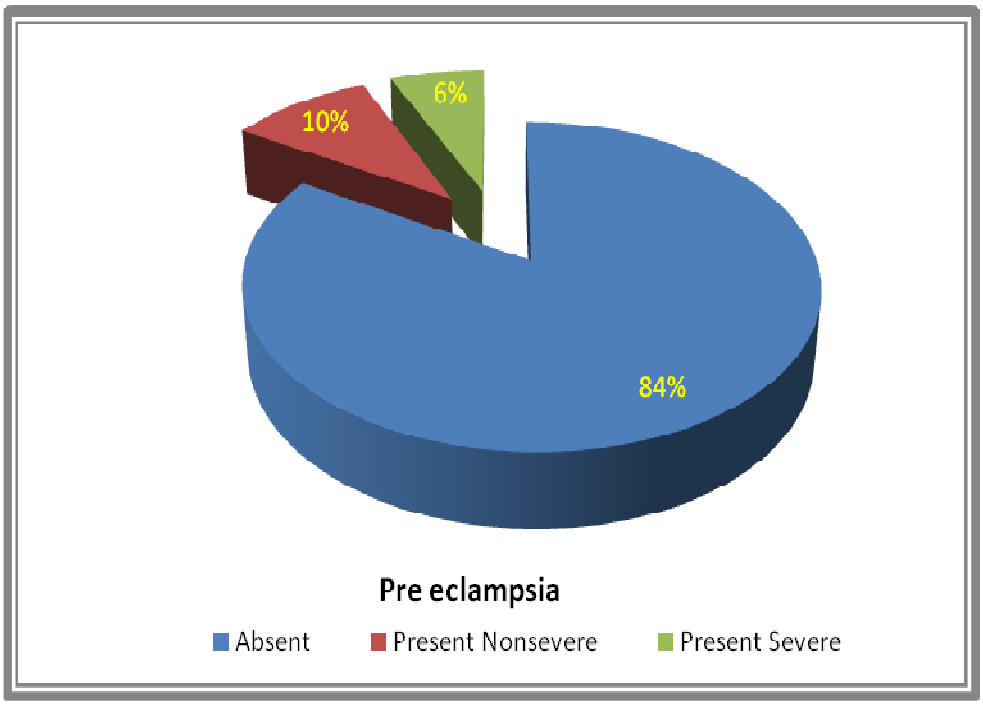
P value < 0.05 → Significant

15 Antenatal women out of 92 women with periodontitis developed preeclampsia and only 5 out of 108 periodontally healthy women developed preeclampsia. This was statistically significant.

PERIODONTITIS ABSENT



PERIODONTITIS PRESENT



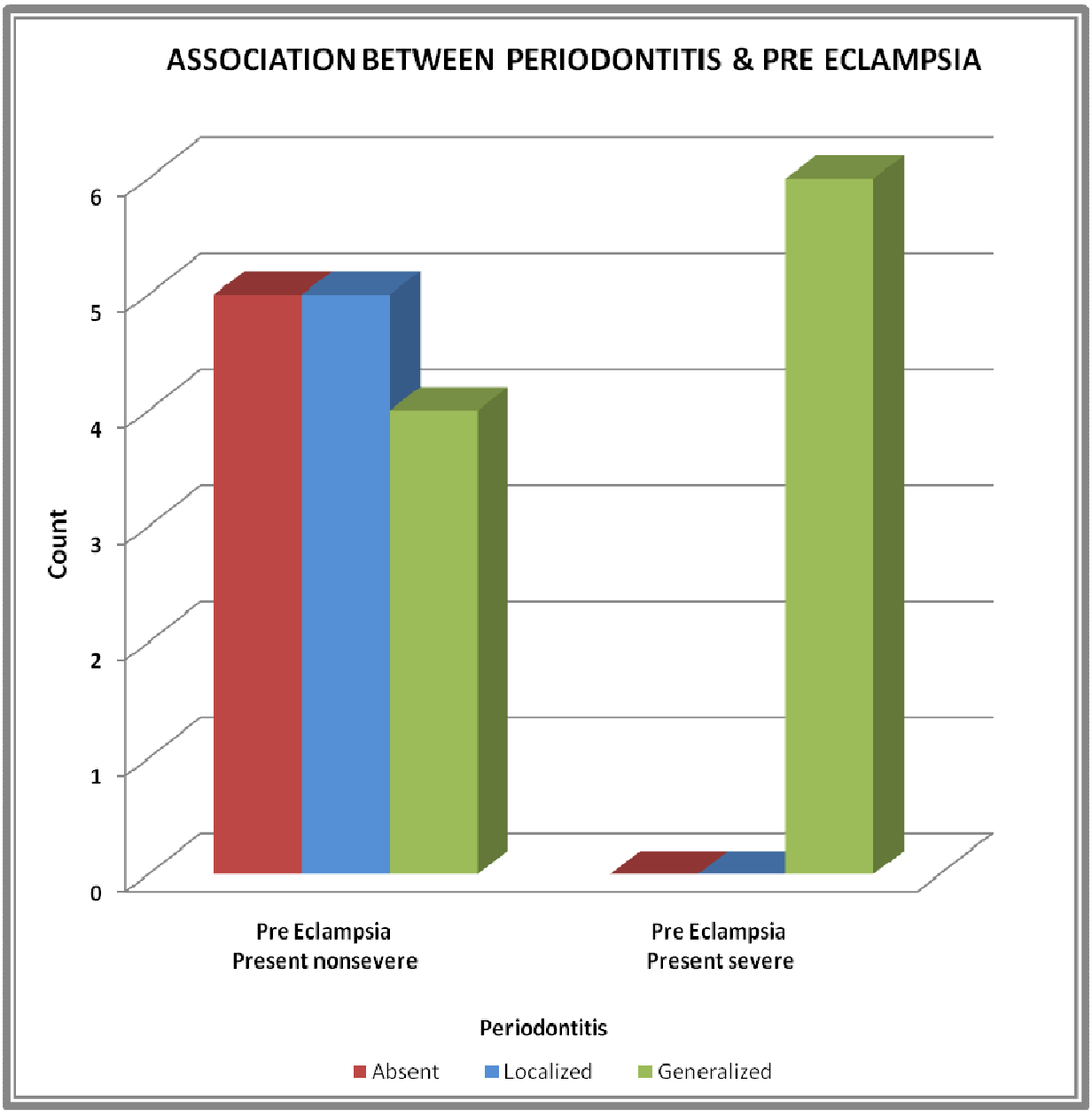
ASSOCIATION BETWEEN PERIODONTITIS & PRE ECLAMPSIA

(Table 4)

Sr No	Pre eclampsia	Periodontitis Absent		Periodontitis Present	
		Number	Percentage	Number	Percentage
1	Absent	103	95.40%	77	83.70%
2	Present Nonsevere	5	4.60%	9	9.78%
3	Present Severe	-	-	6	6.52%

P value < 0.05 → Significant

There is significant statistical association between Periodontitis and Pre eclampsia


ASSOCIATION BETWEEN PERIODONTITIS & PRE ECLAMPSIA
Count
0
1
2
3
4
5
6
Pre Eclampsia
Present nonsevere
Pre Eclampsia
Present severe
Periodontitis
Absent
Localized
Generalized

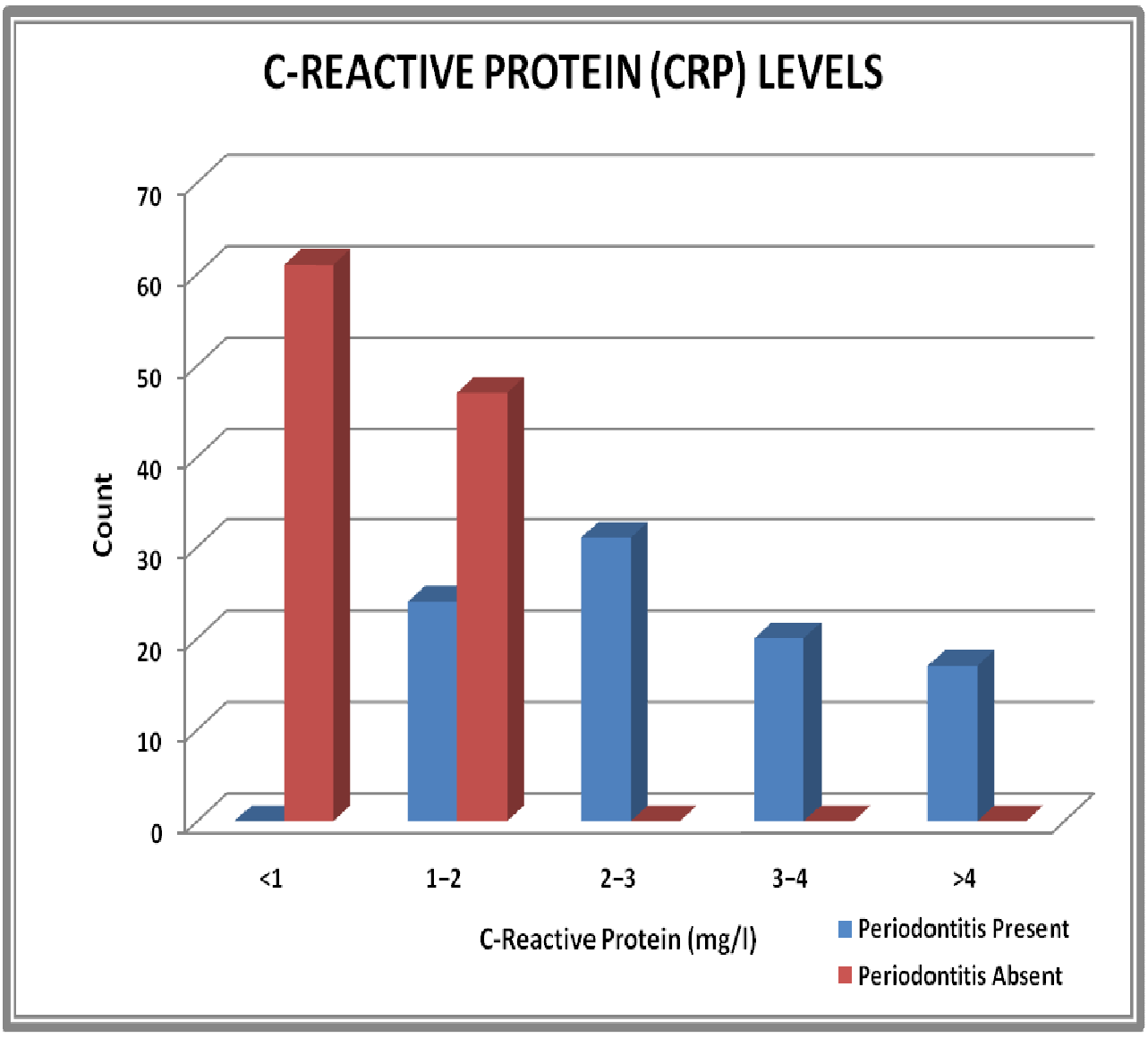
ASSOCIATION BETWEEN PERIODONTITIS & PRE ECLAMPSIA

(Table 5)

PERIODONTITIS	PRE ECLAMPSIA						Total
	Absent		Present Nonsevere		Present Severe		
	Number	Percentage	Number	Percentage	Number	Percentage	
Absent	103	57.22%	5	35.71%	-	-	**108**
Present Localized	49	27.22%	5	35.71%	-	-	**54**
Present Generalized	28	15.56%	4	28.57%	6	100%	**38**
Total	**180**		**14**		**6**		**200**

P value < 0.05 → Significant

All 6 women with severe pre eclampsia had generalized periodontitis, and out of 14 women with non severe pre eclampsia, 5 had localized periodontitis, 4 had generalized periodontitis and 5 women had healthy periodontium.


C-REACTIVE PROTEIN (CRP) LEVELS
Count
70
60
50
40
30
20
10
0
<1
1–2
2–3
3–4
>4
C-Reactive Protein (mg/l)
Periodontitis Present
Periodontitis Absent

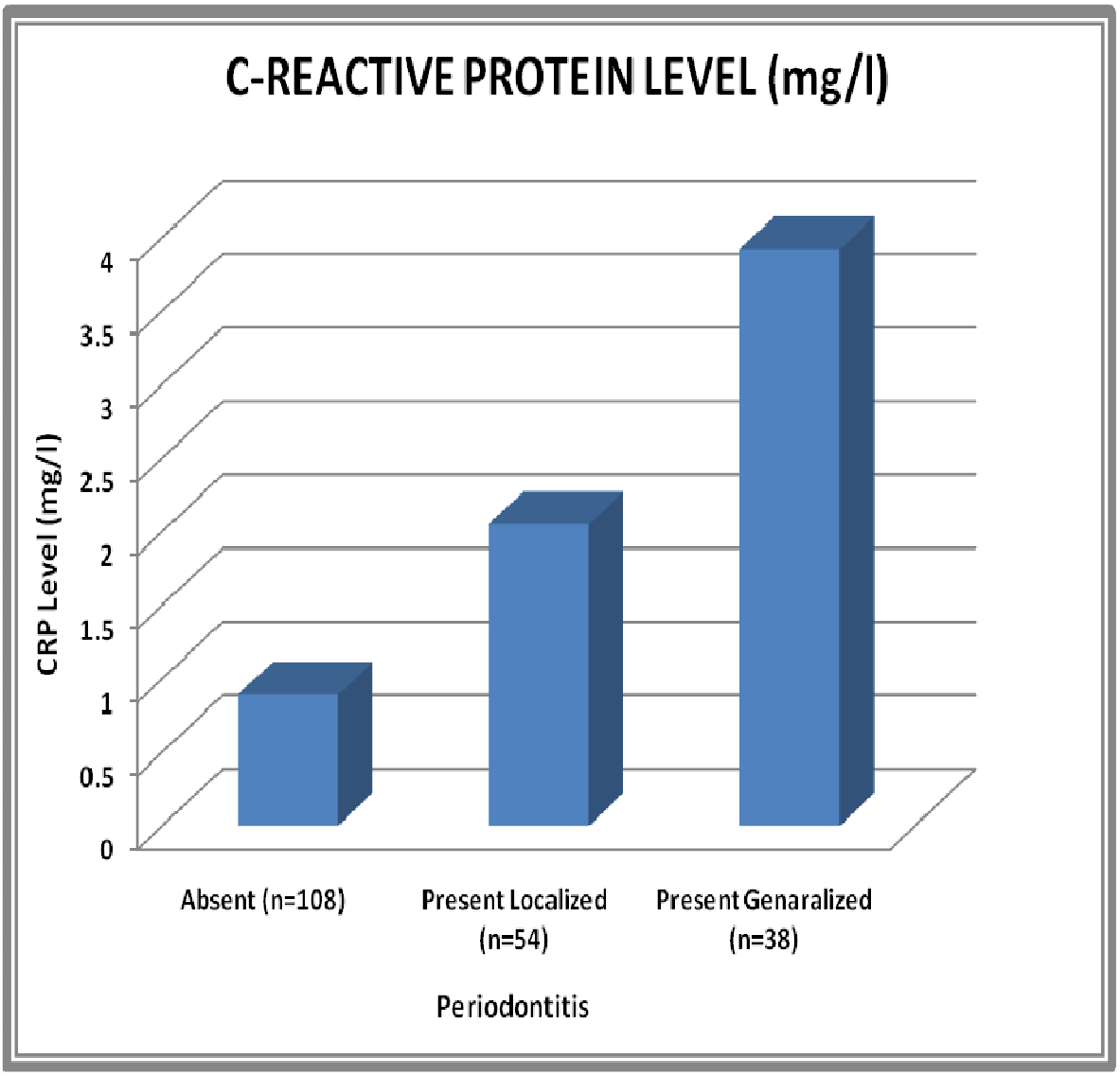
C-REACTIVE PROTEIN (CRP) LEVELS

(Table 6)

Sr No	CRP Level in mg/l	Periodontitis Present		Periodontitis Absent	
		Number	Percentage	Number	Percentage
1	<1	0	1.10%	61	55.56%
2	1−2	24	25%	47	44.44%
3	2−3	31	33.70%	-	-
4	3−4	20	21.73%	-	-
5	>4	17	18.47%	-	-

P value <0.05 → significant

Levels of CRP were greater in women with Periodontitis compared to women with healthy periodontium.


C-REACTIVE PROTEIN LEVEL (mg/l)
CRP Level (mg/l)
4
3.5
3
2.5
2
1.5
1
0.5
0
Absent (n=108)
Present Localized (n=54)
Present Genaralized (n=38)
Periodontitis

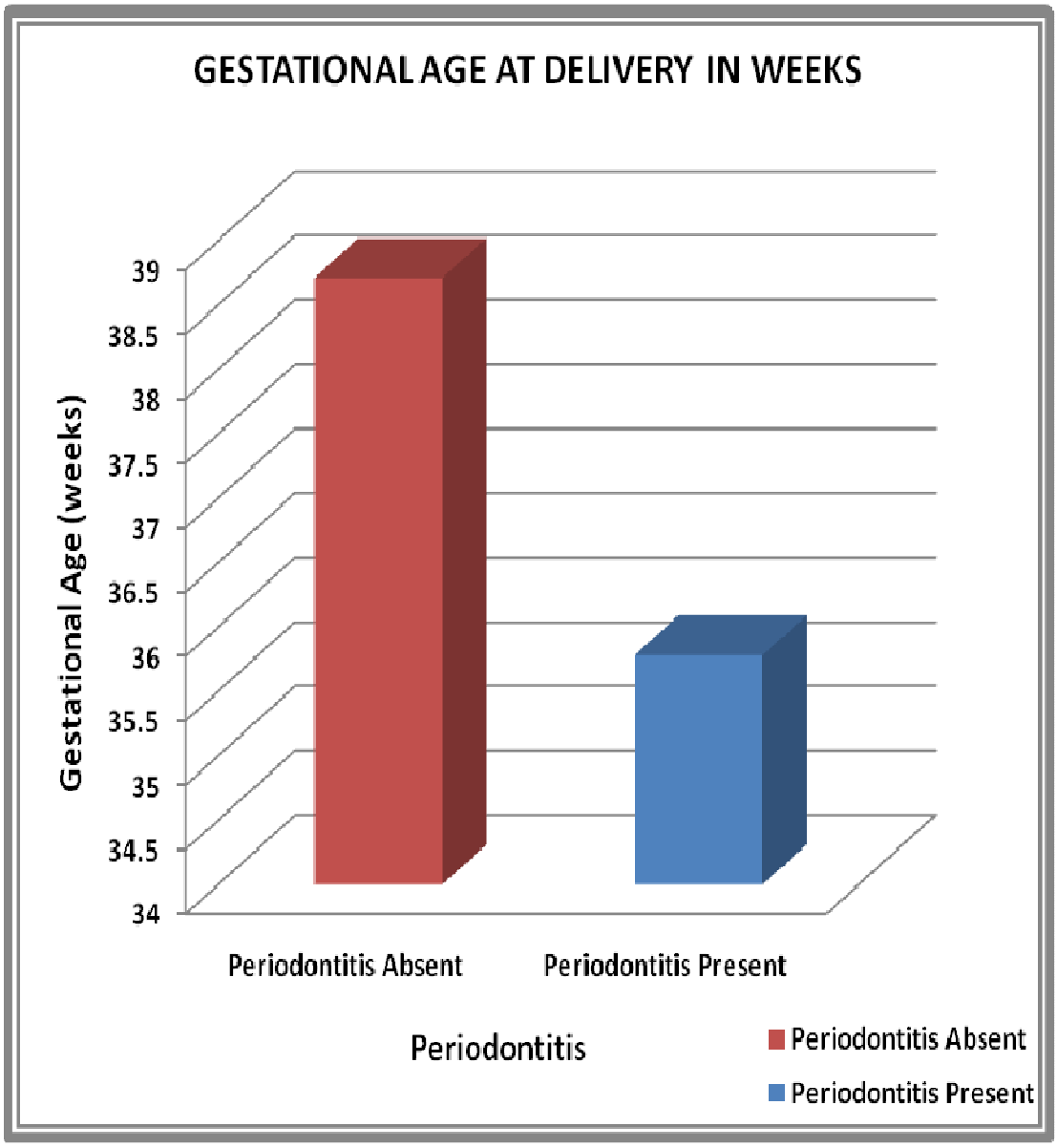
COMPARISON OF CRP LEVELS WITH PERIODONTITIS

(Table 7)

Periodontitis	**CRP level in mg/l**
Absent (n=108)	0.89
Present Localized (n=54)	2.05
Present Genaralized (n=38)	3.92

P value <0.05 → significant

The CRP levels were seen to increase with increasing severity of periodontitis. On applying the anova and post-hoc test, this was found to be statistically significant**.**


GESTATIONAL AGE AT DELIVERY IN WEEKS
Gestational Age (weeks)
39
38.5
38
37.5
37
36.5
36
35.5
35
34.5
34
Periodontitis Absent
Periodontitis Present
Periodontitis
Periodontitis Absent
Periodontitis Present

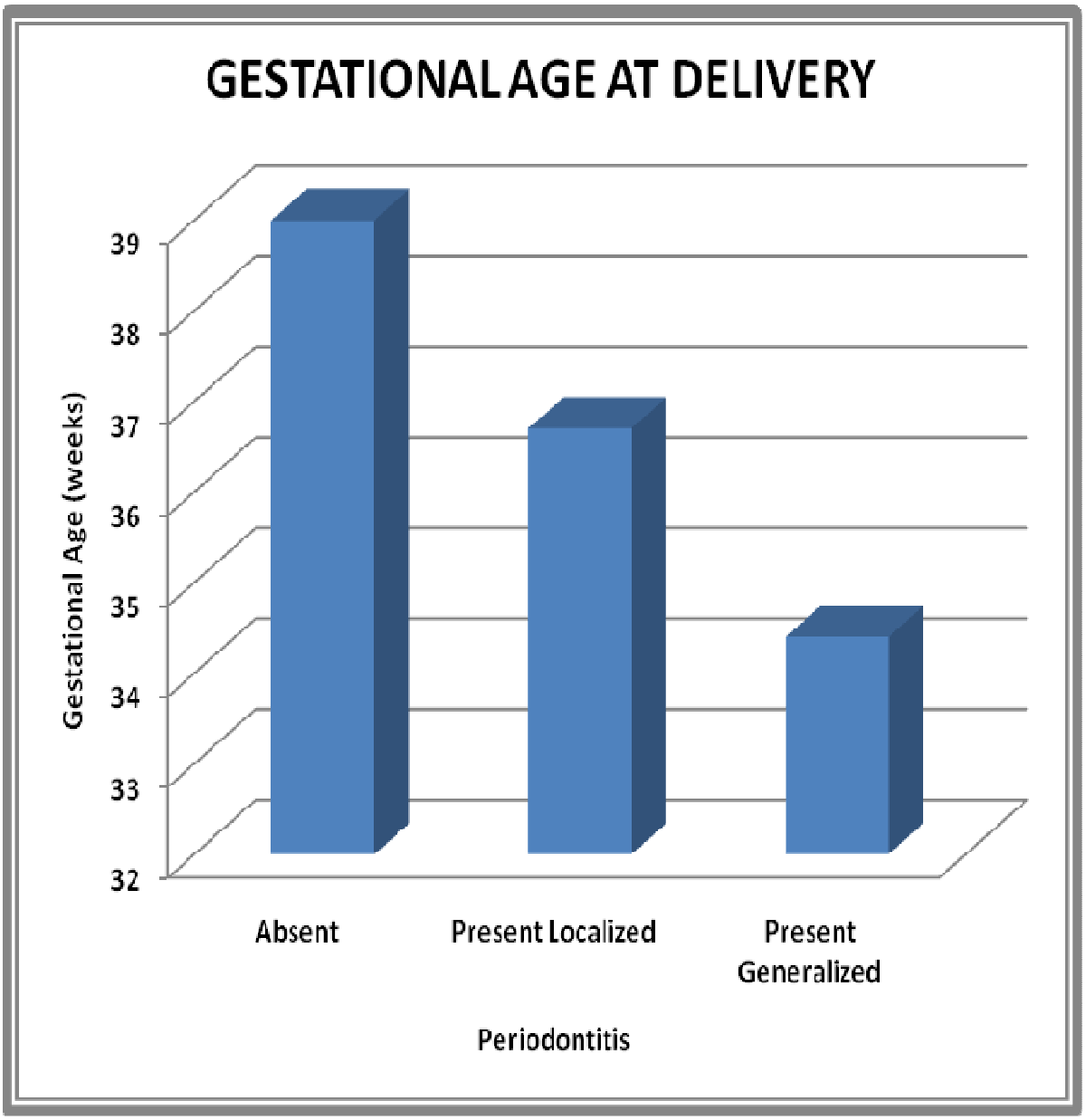
GESTATIONAL AGE AT DELIVERY

(Table 8)

Periodontitis	**Mean gestational age at delivery in weeks**
Absent (n=108)	38.71
Present (n=92)	35.78

P value <0.05 → significant

The Mean gestational age at delivery was 35.78 weeks in women with Periodontitis and 38.71 weeks in women without Periodontitis.


GESTATIONAL AGE AT DELIVERY
Gestational Age (weeks)
39
38
37
36
35
34
33
32
Absent
Present Localized
Present Generalized
Periodontitis

CORRELATION BETWEEN PERIODONTITIS AND GESTATIONAL AGE AT DELIVERY

(Table 9)

Periodontitis	**Mean gestational age at delivery in weeks**
Absent (n=108)	38.7
Present Localized (n=54)	36.7
Present Generalized (n=38)	34.4

P value < 0.05 → Significant

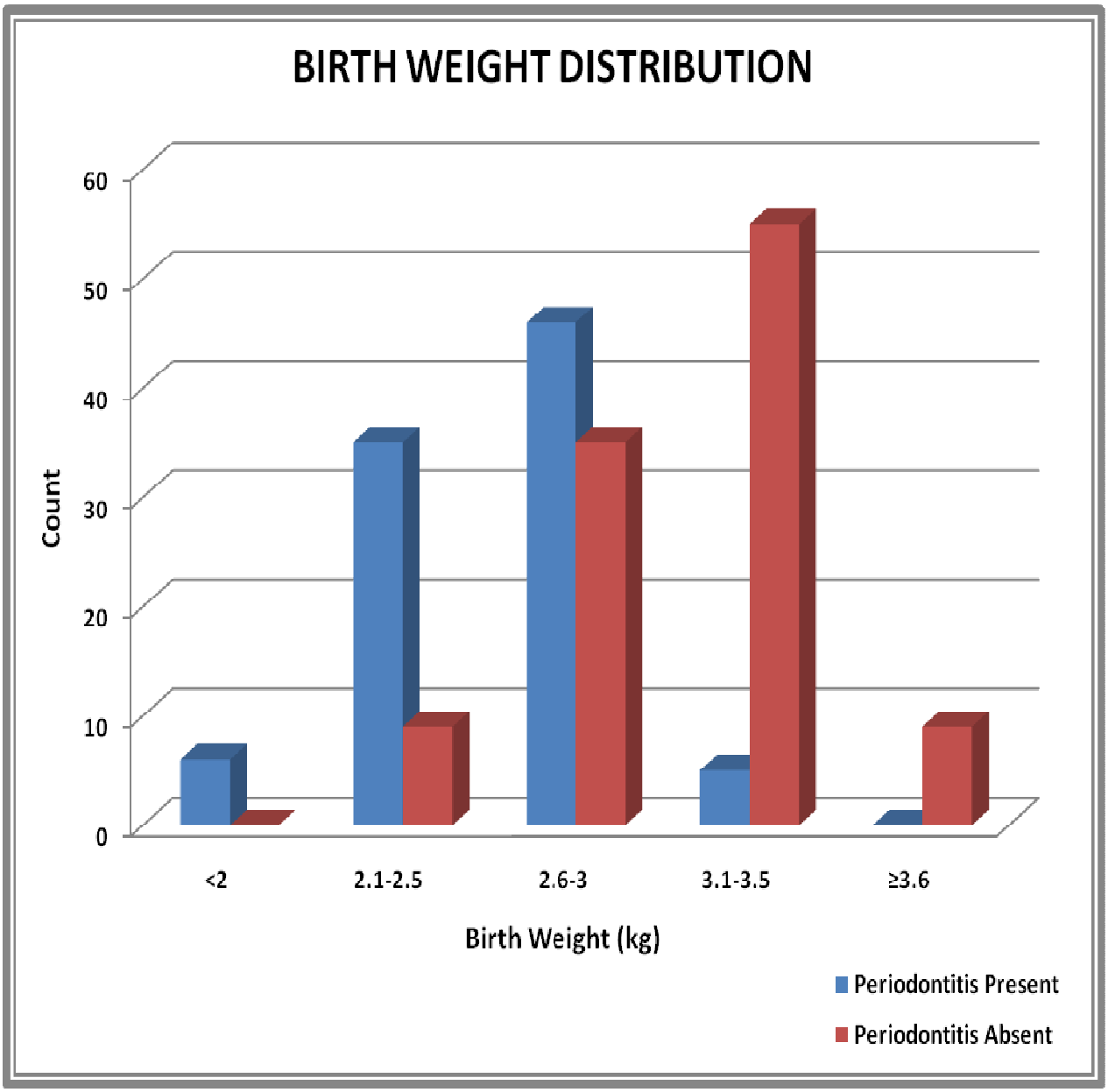
On applying the anova and post-hoc test, this was found to be statistically significant.

CORRELATION BETWEEN DEGREE OF PERIODONTITIS, GESTATIONAL AGE AT DELIVERY AND CRP LEVELS

(Table 10)

Periodontitis	**Mean gestational age at delivery in weeks**	**CRP level in mg/l**
Absent	39	0.89
Present Localized	36.7	2.05
Present Generalized	34.4	3.92

With increase in the severity of periodontitis there was a corresponding increase in CRP level and a decrease in the gestational age at delivery.


BIRTH WEIGHT DISTRIBUTION
60
50
40
30
20
10
0
Count
<2
2.1-2.5
2.6-3
3.1-3.5
≥3.6
Birth Weight (kg)
Periodontitis Present
Periodontitis Absent

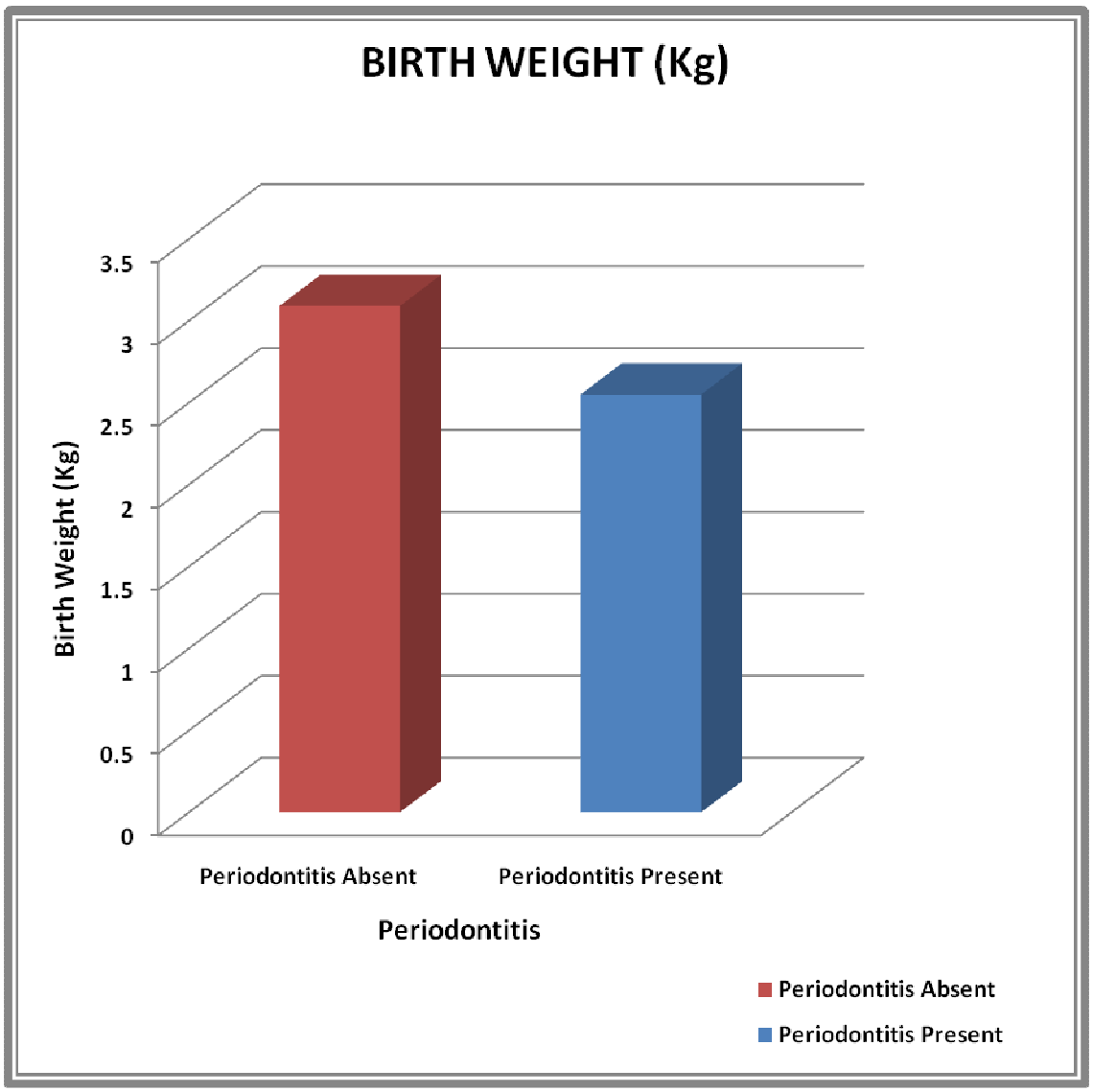
BIRTH WEIGHT DISTRIBUTION

(Table 11)

Sr No	Birth weight (kg)	Periodontitis Present		Periodontitis Absent	
		Number	Percentage	Number	Percentage
1	<2	6	6.52%	0	-
2	2.1-2.5	35	38.04%	9	8.33%
3	2.6-3	46	50%	35	32.41%
4	3.1-3.5	5	5.43%	55	50.93%
5	≥3.6	0	-	9	8.33%

P value <0.05 → Significant

The babies of the mothers with Periodontitis weighed relatively less than babies of mothers without Periodontitis.


BIRTH WEIGHT (Kg)
Birth Weight (Kg)
3.5
3
2.5
2
1.5
1
0.5
0
Periodontitis Absent
Periodontitis Present
Periodontitis
Periodontitis Absent
Periodontitis Present

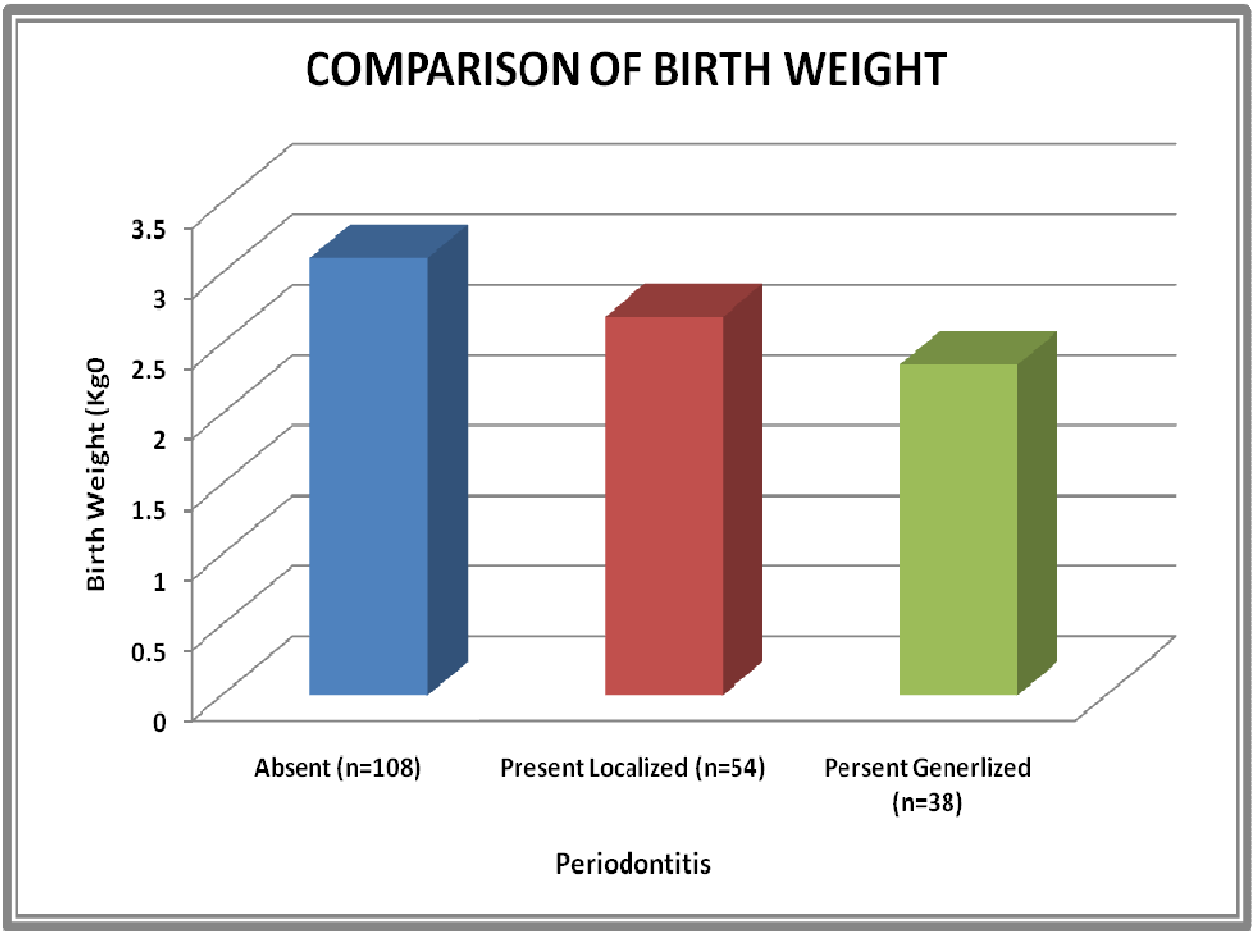
COMPARISON OF BIRTH WEIGHT AND PERIODONTITIS

(Table 12)

Periodontitis	**Count**	**Mean Birth weight (kg)**
Absent	108	3.09
Present	92	2.55

P value <0.05 → Significant

The average birth weight of babies born to mothers with periodontitis was 3.09kg whereas those without periodontitis was 2.55kg


COMPARISON OF BIRTH WEIGHT
Birth Weight (KgO
3.5
3
2.5
2
1.5
1
0.5
0
Absent (n=108)
Present Localized (n=54)
Persent Generlized (n=38)
Periodontitis

COMPARISON OF BIRTH WEIGHT

(Table13)

Periodontitis	**Mean Birth weight (kg)**
Absent (n=108)	3.11
Present Generalized (n=38)	2.35
Present Localized (n=54)	2.69

P value <0.05 → Significant

The birth weights of babies in women with periodontitis were seen to decrease with increasing severity of periodontitis.

On applying the anova and post-hoc test, this was found to be statistically significant**.**

DISCUSSION AND ANALYSIS

. Periodontitis is characterized by exacerbation periods interspersed with periods of remission and presents a local microbial burden that initiates local inflammation and local tissue destruction.

Women with active periodontal disease during pregnancy have transient translocation of oral bacteria to the maternal and fetal blood circulation inciting placental inflammation or oxidative stress early in pregnancy which ultimately produce placental damage and the clinical manifestation of pre eclampsia.

The number of antenatal women originally interviewed and examined for the study was 259 out of which 25 were excluded due to the presence of vaginal / cervical infections, 20 were excluded as they had urinary tract infection and 14 were excluded as they had delivery in non study site. Finally 200 women were recruited for the study.

The mean age of the women in this study was 23 years which was similar to the study conducted by **Contreras et al in 2006[19]** in which it was 24 years.

In this study 23% of the population was in ≤ 20 age group 45% in the age group of 21-25, 28% in the group from 26-30, 3.5% in the age group of 31-35

years. Though extremes of age are risk factors for pre eclampsia relatively fewer belonged to these age groups in the study.

The maximum number of patients was in the 21-25 years age group. This represent the average child bearing age of the women in our country.

Among women with Periodontitis 10.86% of women belong to class IV, 89.13% of women belonged to class V. In periodontally healthy women 5.50% of women belonged to class III, 16.67% of women belonged to class IV and 77.78% of women belonged to class V. Both groups had similar social economic strata distribution and there wasn't significant difference between them.

Over the years in the various studies linking Periodontitis and pre eclampsia a wide array of definitions have been used to describe and quantify the severity of Periodontitis.

The periodontal examination was performed at enrollment and within 48 hours of delivery to determine the presence of severe periodontal disease or periodontal disease progression. It coincide with the study conducted **by Boggess KA et al in 2008[32].**

Offenbacher et al in 1996[44] stated that Periodontitis corresponded to an average clinical attachment loss (CAL) of ≥3mm at ≥60% of the examined site.

Lopez et al in 2002[45] similar to our study examined all the teeth that were present in the dental arch and considered those antenatal women who had at atleast four site with probing depth ≥4mm and clinical attachment loss ≥3mm to be suffering from periodontitis.

Table [no. 3] shows that among the 92 antenatal women with periodontitis 15 (16.3%) developed preeclampsia and out of 108 antenatal women without Periodontitis only 5 (4.6%) developed preeclampsia. The association was statistically significant with a p value < 0.05.

As shown in table 5, out of 14 women with nonsevere pre eclampsia 5 (35.71%) had localized periodontitis, 4(10.53%) women had generalized Periodontitis and 5(35.71%) women were periodontally healthy. All six (100%) women with severe pre eclampsia had generalized Periodontitis.

Out of 180 normotensive women, 103(57.22%) had normal periodontium, 49(27.22%) had localized Periodontitis and 28(15.56%) had generalized Periodontitis. The association between degree of Periodontitis and severity of pre eclampsia was statistically significant with a p value < 0.05. The results of the present study showed that Antenatal women with periodontitis have 3.52 (95% CI = 1.33 – 9.32) times increased risk of developing pre eclampsia.

The association is in concordance with studies carried out in Turkey **(Canaki et al** in 2004)[28], in Colombia (**A.Contreras et al** 2006)[19], Turkey (**Canakci et al** 2007)[35], North carolina (**Boggess et al 2003**)[33], and Brazil (**Fernanda et al** 2008)[31], with ORs varying between 1.94 and 3.78.

Michael Ruma et al in 2008[46] conducted a Cohort study on 775 healty pregnant women who had oral examinations and C-reactive protein levels measured at enrollment (<26 weeks) and found that pre eclampsia was more common in those with high CRP alone (OR 2.6) and those with moderate to severe periodontal disease alone (OR 2.0), but a combination of high CRP levels and moderate to severe periodontal increased the odds ratio to 7.0

As shown in table 6, the C- reactive protein levels were higher in patients with periodontitis. The mean CRP level was 0.89mg/l in antenatal women without periodontitis and 2.82mg/l in those with periodontitis. It was found to assume statistical significance with a P value of <0.05 [Table 7].

This was consistent with the study conducted by **Dr. Pitiphat et al in may 2006**[47] where the median CRP level was 2.23mg/l (interquartile range 0.74 - 4.14) in pregnant women with periodontitis and 1.46mg/l (interquartile range 0.71 – 35.8) in those with no periodontitis.

As has been previously quoted evidence supporting the association between Periodontitis and CRP is based mostly only on studies in men and non-pregnant women. There are only a few studies of Periodontitis and CRP in either pregnant or post-natal women. This is an important area for study because systemic inflammation plays a major role in the pathogenesis of pre eclampsia. CRP might be a plausible mediator of the association between Periodontitis and adverse pregnancy outcome.

As shown in table 7, The CRP levels were found to increase with increasing severity of Periodontitis. In the present study those with generalized periodontitis had the highest elevation of CRP 3.92mg/l (95% CI- 3.8 – 4.05). The one with localized periodontitis had a mean value of 2.05mg/l (95% CI- 1.95 – 2.15). The high CRP level seen in severe periodontitis could well be the cause for pre eclampsia in antenatal women.

As seen in table [8], the mean gestational age at delivery in antenatal women with periodontitis was 35.78 weeks and 38.71 weeks in women without periodontitis.

Further more in the present study the gestational age at delivery was found to be inversely proportional to the degree of periodontitis. In those with localized periodontitis, the mean gestational age at delivery was 36.7 weeks (95%CI= 36.43

– 36.98) and it was 34.7 weeks in case of women with generalized periodontitis (95% CI= 33.99 – 34.98). It was found to be assume statistical significance with a P value of <0.05 [Table 9].

The results of the present study showed that an antenatal woman with Periodontitis have 4.09 [RR=4.09, 95%CI(2.98-5.60) times increased risk of pre term labour. This association is in concordance with that which was originally suggested by **Offenbacher et al** in 1996 [44]and confirmed in further studies carried out in United States (**Offenbacher et al** 1998)[48], Chile (**Lopez et al** 2002)[45], Thailand (**Dasanayake et al** 1998) [46]and Hungary (**Radnai et al** 1998)[47s], with ORs varying between 3.5 and 7.9.

Thus, until recently only cervical / vaginal infections were thought to be capable of triggering inflammatory reactions leading to preterm labour. Data now supports the hypothesis that an inflammatory response to distant infectious foci like Periodontitis is also capable of causing preterm labour.

As shown in Table[11] among antenatal women without periodontitis 8.3% of the babies weight between 2.1-2.5kg, 32.41% of the babies had weight in the range of 2.6-3, 50.93% of the babies had birth weight between 3.1-3.5kg and 8.33% had birth weight >3.5kg.

Among antenatal women with periodontitis 6.52% of the babies had birth weight <2kg, 38.04% of the babies had weight in the range of 2.1 – 2.5 kg. 50% of the babies' weight between 2.6-3kg and 5.43% of the babies had weight in the range between 3.1-3.5kg.

As shown in Table [12], in antenatal women with periodontitis the mean birth weight was 2.55kg and in antenatal women without periodontitis it was 3.09kg.

It was also seen that the mean birth weight also decrease with increasing severity of periodontitis. In generalized periodontitis group the mean birth weight was 2.35kg (95% CI-2.25 – 2.46) and in the localized group the mean birth weight was 2.69kg (95% CI – 2.6-2.75). The values were most significant for generalized Periodontitis with the P value well below 0.05. This agrees with the previous studies which shown an inverse relationship between Periodontitis and birth weight [Table 13].

In conclusion women with maternal periodontal disease and systemic inflammation early in pregnancy as measured by C-reactive protein are at increased risk for the development of pre eclampsia. Larger, more controlled, randomized trials are needed to conclusively prove these links and additional intervention studies are necessary to sdemonstrate the potential systemic benefits

of periodontal therapy so that periodontal therapy may be considered a vital part of prenatal case in pre-eclamptic patients in near future.

These findings indicate that it is in the patient's best interest to include periodontal evaluation as a part of obstetrical and pre-natal care. Individuals with significant pathology could then be offered treatment likely to reduce the incidence of pregnancy complications. Furthermore oral health could be included in pre conceptional conselling so that a lady could begin her pregnancy with a lower risk for pre eclampsia.

For the majority of individuals affected with Periodontitis, the condition is symptom-free until the disease is more advanced. Therefore there is the need for medical personnel to increase the awareness among pregnant women [36]. The American Academy of periodontology recommends that every woman be referred for an oral examination early in pregnancy. The obstetrician should question every woman on symptoms of Periodontitis such as bleeding or swollen gums. Importantly, the present study also provides evidence to support collaborative initiatives among health care providers in medicine and dentistry.

This approach may allow for pregnant women with elevated CRP levels to be classified as "high risk", and thus evaluated more carefully for evidence of adverse oral health and pregnancy outcomes.

Thus both dentists and obstetricians have an obligation to collaborate and co-ordinate efforts to deliver adequate care for women of child bearing age. This transdisciplinary approach though presents unique challenges would reap rich dividends if implemented.

Summary and Conclusion

The study concludes that there is a significant association between periodontitis and pre eclampsia. Antenatal women with periodontitis have 3.52 times increased risk of developing pre eclampsia.

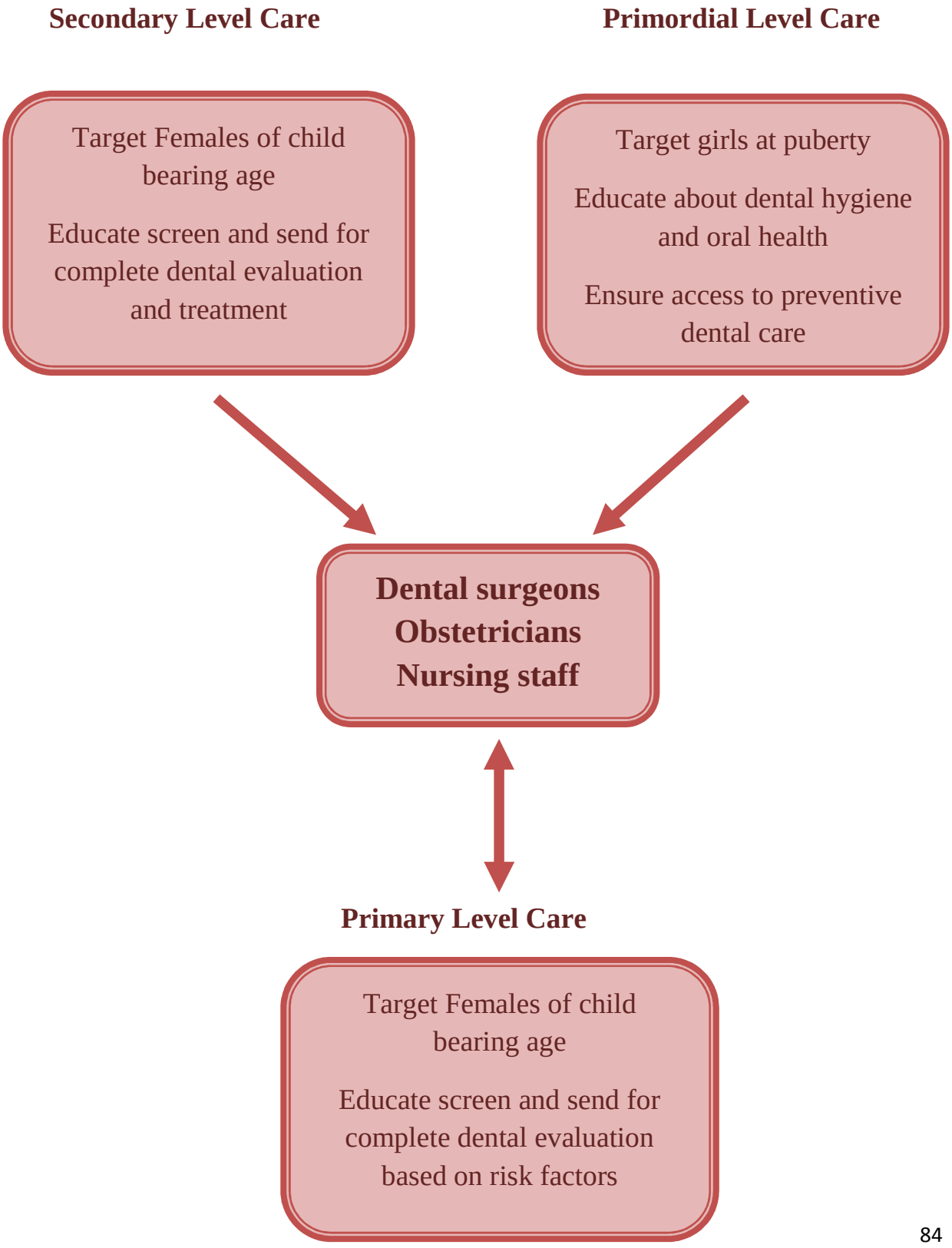
The presence and severity of periodontal disease seems to increase the risk for not only the occurrence but also the severity of pre eclampsia in pregnant women.

The CRP was found to be elevated in antenatal women with Periodontitis when compared to those women who were periodontally healthy. The presence of generalized Periodontitis was associated with lower gestational age at delivery and lower birth weight when compared to presence of localized Periodontitis.

There was significant correlation between increased CRP level, increasing severity of Periodontitis and pre eclampsia. This study also suggests that CRP could be the biologic mediator between the Periodontitis and pre eclampsia.

In conclusion women with maternal periodontal disease and systemic inflammation early in pregnancy as measured by C - reactive protein are at increased risk for the development of pre eclampsia. If the future studies with larger sample show that the treatments of periodontal infections substantially reduce the risk of pre eclampsia as is the case with other adverse pregnancy outcome then periodontal therapy may be considered a vital part of prenatal care in pre-eclamptic patient

INTERDISCIPLINARY PREVENTIVE CARE



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PROFORMA

Name: Last menstrual period:

Age: Expected date of delivery:

I.P.Number:

Gestational age(weeks):

Gestational age as per 1 st trimester ultra sonogram:

Socio-Economic Class:

Educational Qualification:

Menstrual history:

Marital history:

Obstetrics history:

Medical illness:

H/o excessive foul smelling vaginal discharge:

H/o Diabetes/heart disease/hypertension/PIH/multiple gestation:

H/o any tooth extraction in the past:

H/o toothache/bleeding from gum

Examination

General Examination:

Temperature:

Pulse:

Blood Pressure:

Per abdomen Examination:

Speculum Examination:

Biochemical and Microbiological Investigations:

Hb %:

Platelets:

Blood Sugar:

Blood Urea:

Sr creatinine:

Liver function test:

Sr.uric acid:

C-Reactive protein Level:

Urine for Culture:

KOH whiff test for Bacterial Vaginosis:

Wet Mount Examination:

ULTRASONOGRAM:

Results of Periodontal Examination:

Periodontitis: Present/Absent

If present: Localized/Generalized

Degree of Periodontitis: Mild/Moderate/Severe

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis
1	Valarmathi	21	9418	V	03/11/2008	10/08/2009	26	0.59	Absent	Absent
2	Latha	20	10075	V	25/11/2008	01/09/2009	23	1.02	Absent	Absent
3	Vasuki	18	9856	V	23/11/2008	30/08/2009	24	1.03	Absent	Absent
4	kala	27	9491	V	05/11/2008	12/08/2009	26	1.56	Absent	Present Localized
5	Geetha	21	9710	V	20/11/2008	27/08/2009	24	0.69	Absent	Absent
6	Rajeshwari	32	9272	V	29/10/2008	05/08/2009	26	1.8	Absent	Present Localized
7	Reshma	21	9345	V	29/10/2008	05/08/2009	27	1.01	Absent	Absent
8	Firdose begaum	28	9199	V	26/10/2008	02/08/2009	28	1.01	Absent	Present Localized
9	shahin beguam	26	9637	V	15/11/2008	22/08/2009	26	3.9	Absent	Present Generalized
10	Devi	30	10002	V	24/11/2008	31/08/2009	24	0.53	Absent	Absent
11	Jeya	26	9126	V	23/10/2008	30/07/2009	28	1.83	Absent	Present Localized
12	vinnarasi	22	9783	V	20/11/2008	27/08/2009	22	4.1	Present severe	Present Generalized
13	Pramila	26	9929	IV	23/11/2008	30/08/2009	24	3.58	Absent	Present Generalized
14	Nazeema	24	9564	V	07/11/2008	14/08/2009	26	1.47	Absent	Present Localized
15	Malini gracy	23	10440	V	20/12/2008	27/09/2009	20	1.02	Absent	Absent
16	Muniamma	25	10294	V	08/12/2008	14/09/2009	22	3.78	Absent	Present Generalized
17	Lalitha	30	10148	IV	02/12/2008	09/09/2009	24	1.12	Absent	Absent
18	Ragavi	28	10367	V	19/12/2008	26/09/2009	26	1.67	Absent	Present Localized
19	Mariammal	19	10221	V	04/12/2008	11/09/2009	24	0.51	Absent	Absent
20	Devipriya	20	301	V	01/02/2009	08/11/2009	20	0.73	Absent	Absent
21	Geetha	23	10513	V	21/12/2008	28/09/2009	26	3.8	Absent	Present Generalized
22	Lalitha	29	405	V	04/03/2009	11/12/2009	24	0.67	Absent	Absent
23	Rosy	26	639	IV	19/03/2009	26/12/2009	22	0.94	Absent	Absent
24	Shenbagavalli	26	327	V	19/02/2009	26/11/2009	26	3.84	Absent	Present Generalized
25	Hemavathy	27	457	V	06/03/2009	13/12/2009	24	1.78	Absent	Present Localized
26	Poogothai	32	1107	V	05/04/2009	12/01/2010	20	0.65	Absent	Absent
27	Keerthana	22	717	V	22/03/2009	29/12/2009	22	0.57	Absent	Absent
28	Alima	23	743	V	22/03/2009	29/12/2009	22	2.02	Absent	Present Localized
29	Janaki	23	1133	IV	06/04/2009	13/01/2010	20	4.1	Absent	Present Generalized
30	Vijayalakshmi	23	509	V	09/03/2009	16/12/2009	24	1.97	Absent	Present Localized

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis	ional age at delivery	Birth Weight (Kg)
1	Valarmathi	21	9418	V	03/11/2008	10/08/2009	26	0.59	Absent	Absent	38	3.1
2	Latha	20	10075	V	25/11/2008	01/09/2009	23	1.02	Absent	Absent	39	2.9
3	Vasuki	18	9856	V	23/11/2008	30/08/2009	24	1.03	Absent	Absent	39	3.2
4	kala	27	9491	V	05/11/2008	12/08/2009	26	1.56	Absent	Present Localized	36	2.75
5	Geetha	21	9710	V	20/11/2008	27/08/2009	24	0.69	Absent	Absent	39	3.32
6	Rajeshwari	32	9272	V	29/10/2008	05/08/2009	26	1.8	Absent	Present Localized	37	2.7
7	Reshma	21	9345	V	29/10/2008	05/08/2009	27	1.01	Absent	Absent	40	3.2
8	Firdose begaum	28	9199	V	26/10/2008	02/08/2009	28	1.01	Absent	Present Localized	37	2.7
9	shahin beguam	26	9637	V	15/11/2008	22/08/2009	26	3.9	Absent	Present Generalized	35	2.4
10	Devi	30	10002	V	24/11/2008	31/08/2009	24	0.53	Absent	Absent	40	3.3
11	Jeya	26	9126	V	23/10/2008	30/07/2009	28	1.83	Absent	Present Localized	36	2.8
12	vinnarasi	22	9783	V	20/11/2008	27/08/2009	22	4.1	Present severe	Present Generalized	33	2
13	Pramila	26	9929	IV	23/11/2008	30/08/2009	24	3.58	Absent	Present Generalized	35	2.4
14	Nazeema	24	9564	V	07/11/2008	14/08/2009	26	1.47	Absent	Present Localized	36	2.6
15	Malini gracy	23	10440	V	20/12/2008	27/09/2009	20	1.02	Absent	Absent	40	3.4
16	Muniamma	25	10294	V	08/12/2008	14/09/2009	22	3.78	Absent	Present Generalized	36	2.7
17	Lalitha	30	10148	IV	02/12/2008	09/09/2009	24	1.12	Absent	Absent	40	3.1
18	Ragavi	28	10367	V	19/12/2008	26/09/2009	26	1.67	Absent	Present Localized	36	2.5
19	Mariammal	19	10221	V	04/12/2008	11/09/2009	24	0.51	Absent	Absent	39	3.1
20	Devipriya	20	301	V	01/02/2009	08/11/2009	20	0.73	Absent	Absent	39	3.8
21	Geetha	23	10513	V	21/12/2008	28/09/2009	26	3.8	Absent	Present Generalized	35	2.6
22	Lalitha	29	405	V	04/03/2009	11/12/2009	24	0.67	Absent	Absent	38	3.5
23	Rosy	26	639	IV	19/03/2009	26/12/2009	22	0.94	Absent	Absent	38	3.75
24	Shenbagavalli	26	327	V	19/02/2009	26/11/2009	26	3.84	Absent	Present Generalized	35	2.6
25	Hemavathy	27	457	V	06/03/2009	13/12/2009	24	1.78	Absent	Present Localized	37	2.9
26	Poogothai	32	1107	V	05/04/2009	12/01/2010	20	0.65	Absent	Absent	37	3.05
27	Keerthana	22	717	V	22/03/2009	29/12/2009	22	0.57	Absent	Absent	38	3.3
28	Alima	23	743	V	22/03/2009	29/12/2009	22	2.02	Absent	Present Localized	37	2.65
29	Janaki	23	1133	IV	06/04/2009	13/01/2010	20	4.1	Absent	Present Generalized	36	2.7
30	Vijayalakshmi	23	509	V	09/03/2009	16/12/2009	24	1.97	Absent	Present Localized	38	3.1

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis	Gestational age at delive	Birth Weight (Kg)
31	Amudha	22	1159	V	08/04/2009	15/01/2010	20	3.86	Absent	Present Generalized	35	2.5
32	Dhanalakshmi	22	821	V	25/03/2009	01/01/2010	22	3.85	Absent	Present Generalized	35	2.6
33	Saranya	20	353	V	24/02/2009	03/12/2009	26	3.89	Absent	Present Generalized	36	2.5
34	Naramada devi	21	561	IV	12/03/2009	19/12/2009	24	4.02	Absent	Present Generalized	35	2.6
35	Priya darshni	23	691	V	21/03/2009	28/12/2009	23	0.81	Absent	Absent	37	2.9
36	Mosina	29	899	V	28/03/2009	03/01/2010	22	4.1	Absent	Present Generalized	36	2.5
37	Kavitha	21	1263	IV	14/04/2009	21/01/2010	20	3.96	Absent	Present Generalized	36	2.6
38	Anzarbevi	19	379	V	03/03/2009	10/12/2009	26	2.11	Absent	Present Localized	37	2.9
39	Hema	24	613	V	16/03/2009	23/12/2009	24	2.01	Absent	Present Localized	37	2.7
40	Divya	21	847	V	25/03/2009	01/01/2010	23	3.76	Absent	Present Generalized	35	2.6
41	Eswari	22	431	V	05/03/2009	12/12/2009	26	2.73	Present nonsevere	Present Localized	36	2.5
42	Bakiyalakshmi	21	665	V	19/03/2009	26/12/2009	24	1.01	Absent	Absent	38	3.25
43	Dhanalakshmi	20	1419	V	18/04/2009	25/01/2010	20	4.38	Present nonsevere	Present Generalized	33	2.3
44	Shameem	27	1081	V	04/04/2009	11/01/2010	22	1.02	Absent	Absent	37	3.25
45	Thenmozhi	22	795	IV	23/03/2009	30/12/2009	24	1.03	Absent	Absent	38	3.3
46	Komalavalli	24	535	V	10/03/2009	17/12/2009	26	4.2	Present nonsevere	Present Generalized	34	2.2
47	chithra	21	483	V	08/03/2009	15/12/2009	26	1.15	Present nonsevere	Absent	35	2.4
48	Durga	22	1211	V	10/04/2009	17/01/2010	22	0.72	Absent	Absent	37	3.7
49	Hemalatha	20	587	V	15/03/2009	22/12/2009	26	2.95	Absent	Present Generalized	36	2.7
50	Kanchana	25	1003	V	30/03/2009	06/01/2010	24	0.62	Absent	Absent	37	3.5
51	Nandhini	19	951	V	29/03/2009	05/01/2010	25	3.99	Present severe	Present Generalized	34	2.1
52	Gowri	24	1705	V	29/04/2009	06/02/2010	20	0.66	Absent	Absent	38	3.5
53	Shamshad	23	1367	V	17/04/2009	24/01/2010	22	0.67	Absent	Absent	39	3.2
54	Yasmin Begam	24	1055	V	03/04/2009	10/01/2010	24	0.78	Absent	Absent	38	3.3
55	Nirmala	20	1445	V	19/04/2009	26/01/2010	22	0.69	Absent	Absent	39	3.4
56	Salma	20	769	IV	22/03/2009	29/12/2009	26	1.01	Absent	Absent	39	3.5
57	Usha	24	977	V	29/03/2009	05/01/2010	25	3.15	Absent	Present Generalized	36	2.7
58	Kamtchi	21	873	V	25/03/2009	01/01/2010	26	0.66	Absent	Absent	40	3.2
59	Kavitha	34	1185	V	09/04/2009	16/01/2010	24	0.72	Absent	Absent	38	3.1
60	selvi	20	1393	V	18/04/2009	25/01/2010	23	2.62	Present nonsevere	Present Localized	34	2.3

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis	Gestational age at delive	Birth Weight (Kg)
61	Karpagam	24	1627	V	26/04/2009	03/02/2010	22	1.02	Absent	Absent	37	3.25
62	Lakshmi	24	925	V	28/03/2009	04/01/2010	26	1.05	Absent	Absent	37	3.5
63	Parameshwari	22	1029	IV	02/04/2009	09/01/2010	26	3.9	Absent	Present Generalized	36	2.6
64	Kamatchi	26	1341	V	15/04/2009	22/01/2010	24	1.52	Absent	Present Localized	37	2.9
65	shakira	24	1731	IV	02/05/2009	09/02/2010	22	1.6	Absent	Absent	37	3.65
66	Revathy	23	2147	III	16/05/2009	22/02/2010	20	1.09	Absent	Absent	39	3.15
67	Bhavani	24	1809	IV	05/05/2009	12/02/2010	22	1.87	Absent	Present Localized	37	2.8
68	Devaki	24	1575	V	23/04/2009	30/01/2010	24	2.1	Absent	Present Localized	36	2.68
69	Bhuvaneshwari	23	1887	V	07/05/2009	14/02/2010	22	0.78	Absent	Absent	39	3.25
70	Tamilinbam	23	1237	V	10/04/2009	17/01/2010	26	3.05	Absent	Present Generalized	36	2.75
71	Shahina	26	2095	V	11/05/2009	18/02/2010	22	4.01	Absent	Present Generalized	36	2.4
72	Thamarai	27	1289	V	14/04/2009	21/01/2010	26	2.21	Absent	Present Localized	37	2.8
73	Sangeetha	28	1315	IV	14/04/2009	21/01/2010	26	1.98	Absent	Present Localized	37	2.9
74	sarasu	26	1679	V	27/04/2009	04/02/2010	24	1.97	Absent	Present Localized	36	2.88
75	Kavitha	26	2641	V	30/05/2009	06/03/2010	20	0.68	Absent	Absent	39	3.15
76	ilakiya	28	3057	V	15/06/2009	22/03/2010	18	0.71	Absent	Absent	39	3.28
77	chithra	30	2745	V	02/06/2009	09/03/2010	20	1.88	Absent	Present Localized	37	2.7
78	Silambarasi	26	2121	V	14/05/2009	21/02/2010	23	3.7	Absent	Present Generalized	35	2.3
79	Kirupa	24	1549	V	22/04/2009	29/01/2010	26	3.8	Absent	Present Generalized	36	2.5
80	Noornisha	20	1497	V	20/04/2009	27/01/2010	24	4.13	Present nonsevere	Present Generalized	32	1.9
81	Nalani	19	3551	V	06/07/2009	13/04/2010	20	1.01	Absent	Absent	40	3.25
82	Radha	22	2459	V	23/05/2009	02/03/2010	22	0.64	Absent	Absent	40	3.9
83	Kamala	24	1991	V	08/05/2009	15/02/2010	24	0.89	Absent	Absent	40	3.5
84	Sara	21	2485	V	24/05/2009	03/03/2010	22	0.65	Absent	Absent	40	3.25
85	Ajantha	26	3005	V	13/06/2009	20/03/2010	24	1.78	Absent	Present Localized	35	2.4
86	Dhanalakshmi	24	2693	V	31/05/2009	07/03/2010	26	2.2	Absent	Present Localized	36	2.5
87	Kalaivani	26	2771	IV	02/06/2009	09/03/2010	26	0.73	Absent	Absent	40	3.6
88	Sriduja	22	3109	V	18/06/2009	25/03/2010	24	2.55	Absent	Present Localized	36	2.6
89	Radhika	24	3733	IV	17/07/2009	24/04/2010	20	0.96	Absent	Absent	40	2.95
90	Bharani	19	3265	V	27/06/2009	03/04/2010	23	4.97	Present severe	Present Generalized	33	2.25

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis	Gestational age at delive	Birth Weight (Kg)
91	Sarala	19	3135	V	18/06/2009	25/03/2010	20	1.02	Absent	Absent	40	3
92	Amul	20	3161	V	18/06/2009	25/03/2010	22	0.561	Absent	Absent	40	2.98
93	Sumitha	26	2875	V	11/06/2009	18/03/2010	23	0.91	Absent	Absent	40	3.75
94	Mallika Begaum	27	2355	V	19/05/2009	26/02/2010	26	0.42	Absent	Absent	40	3.1
95	Radha	26	2225	IV	17/05/2009	24/02/2010	26	0.66	Absent	Absent	40	2.9
96	Abitha	24	2043	V	10/05/2009	17/02/2010	27	2.01	Absent	Present Localized	38	2.9
97	Vimala	19	2589	V	27/05/2009	03/03/2010	25	4.2	Present severe	Present Generalized	30	1.4
98	Renuka devi	27	2511	V	27/05/2009	03/03/2010	24	2.24	Absent	Present Localized	36	2.7
99	Asma	26	2381	IV	20/05/2009	27/02/2010	25	0.89	Absent	Absent	40	2.95
100	Gomathy Rajesh	21	2069	V	10/05/2009	17/02/2010	26	2.23	Absent	Present Localized	36	2.5
101	Geethalakshmi	19	2303	V	18/05/2009	25/02/2010	25	1.12	Absent	Absent	40	3.43
102	Shyamala	28	1471	V	19/04/2009	26/01/2010	28	0.89	Absent	Absent	40	2.75
103	Rahini	21	1835	V	05/05/2009	12/02/2010	26	3.97	Absent	Present Generalized	35	2.5
104	Sharmila	26	1913	V	07/05/2009	14/02/2010	26	0.46	Absent	Absent	40	3.5
105	Annapoorani	20	2537	V	24/05/2009	03/03/2010	23	2.02	Absent	Present Localized	38	2.8
106	Nazeema	26	1653	IV	26/04/2009	03/02/2010	26	1.31	Absent	Absent	40	2.9
107	Bharani	22	2953	V	12/06/2009	19/03/2010	24	1.4	Absent	Absent	40	2.8
108	Thakira	25	2563	V	27/05/2009	03/03/2010	22	1.8	Absent	Absent	40	3.55
109	Saritha	21	2979	V	12/06/2009	19/03/2010	28	1.1	Absent	Absent	40	3
110	Hemavathy	29	1757	III	03/05/2009	10/02/2010	26	1.02	Absent	Absent	40	3.47
111	Krishnveni	30	2797	V	08/06/2009	15/03/2010	22	4.59	Present nonsevere	Present Generalized	35	2.5
112	Nasrin	21	3187	V	20/06/2009	27/03/2010	20	1.78	Absent	Present Localized	38	3.1
113	Eswari	19	2823	V	09/06/2009	16/03/2010	22	2.17	Absent	Present Localized	37	3
114	Vijaylakshmi	20	1601	V	24/04/2009	31/01/2010	28	2.16	Absent	Present Localized	39	3.01
115	Vasanthi	22	2017	V	09/05/2009	15/02/2010	26	2.19	Absent	Present Localized	37	2.81
116	Datchayani	21	1965	V	08/05/2009	15/02/2010	26	4.05	Absent	Present Generalized	34	2.35
117	Nirmala	22	1939	V	07/05/2009	14/02/2010	26	0.66	Absent	Absent	40	3.3
118	Divya	26	2433	V	21/05/2009	28/02/2010	24	1.35	Absent	Absent	40	2.85
119	Saranya	20	1523	V	21/04/2009	28/01/2010	28	1.1	Absent	Absent	40	2.8
120	Dhanalakshmi	29	2407	V	20/05/2009	27/02/2010	22	1.45	Absent	Absent	40	3.1

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91	Sarala	19	3135	V	18/06/2009	25/03/2010	20	1.02	Absent	Absent	40	3
92	Amul	20	3161	V	18/06/2009	25/03/2010	22	0.561	Absent	Absent	40	2.98
93	Sumitha	26	2875	V	11/06/2009	18/03/2010	23	0.91	Absent	Absent	40	3.75
94	Mallika Begaum	27	2355	V	19/05/2009	26/02/2010	26	0.42	Absent	Absent	40	3.1
95	Radha	26	2225	IV	17/05/2009	24/02/2010	26	0.66	Absent	Absent	40	2.9
96	Abitha	24	2043	V	10/05/2009	17/02/2010	27	2.01	Absent	Present Localized	38	2.9
97	Vimala	19	2589	V	27/05/2009	03/03/2010	25	4.2	Present severe	Present Generalized	30	1.4
98	Renuka devi	27	2511	V	27/05/2009	03/03/2010	24	2.24	Absent	Present Localized	36	2.7
99	Asma	26	2381	IV	20/05/2009	27/02/2010	25	0.89	Absent	Absent	40	2.95
100	Gomathy Rajesh	21	2069	V	10/05/2009	17/02/2010	26	2.23	Absent	Present Localized	36	2.5
101	Geethalakshmi	19	2303	V	18/05/2009	25/02/2010	25	1.12	Absent	Absent	40	3.43
102	Shyamala	28	1471	V	19/04/2009	26/01/2010	28	0.89	Absent	Absent	40	2.75
103	Rahini	21	1835	V	05/05/2009	12/02/2010	26	3.97	Absent	Present Generalized	35	2.5
104	Sharmila	26	1913	V	07/05/2009	14/02/2010	26	0.46	Absent	Absent	40	3.5
105	Annapoorani	20	2537	V	24/05/2009	03/03/2010	23	2.02	Absent	Present Localized	38	2.8
106	Nazeema	26	1653	IV	26/04/2009	03/02/2010	26	1.31	Absent	Absent	40	2.9
107	Bharani	22	2953	V	12/06/2009	19/03/2010	24	1.4	Absent	Absent	40	2.8
108	Thakira	25	2563	V	27/05/2009	03/03/2010	22	1.8	Absent	Absent	40	3.55
109	Saritha	21	2979	V	12/06/2009	19/03/2010	28	1.1	Absent	Absent	40	3
110	Hemavathy	29	1757	III	03/05/2009	10/02/2010	26	1.02	Absent	Absent	40	3.47
111	Krishnveni	30	2797	V	08/06/2009	15/03/2010	22	4.59	Present nonsevere	Present Generalized	35	2.5
112	Nasrin	21	3187	V	20/06/2009	27/03/2010	20	1.78	Absent	Present Localized	38	3.1
113	Eswari	19	2823	V	09/06/2009	16/03/2010	22	2.17	Absent	Present Localized	37	3
114	Vijaylakshmi	20	1601	V	24/04/2009	31/01/2010	28	2.16	Absent	Present Localized	39	3.01
115	Vasanthi	22	2017	V	09/05/2009	15/02/2010	26	2.19	Absent	Present Localized	37	2.81
116	Datchayani	21	1965	V	08/05/2009	15/02/2010	26	4.05	Absent	Present Generalized	34	2.35
117	Nirmala	22	1939	V	07/05/2009	14/02/2010	26	0.66	Absent	Absent	40	3.3
118	Divya	26	2433	V	21/05/2009	28/02/2010	24	1.35	Absent	Absent	40	2.85
119	Saranya	20	1523	V	21/04/2009	28/01/2010	28	1.1	Absent	Absent	40	2.8
120	Dhanalakshmi	29	2407	V	20/05/2009	27/02/2010	22	1.45	Absent	Absent	40	3.1

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151	Anjali	24	3577	IV	06/07/2009	13/04/2010	26	0.78	Absent	Absent	39	3.1
152	Maaya	26	4160	V	01/08/2009	08/05/2010	22	0.97	Absent	Absent	39	2.9
153	Parvathi	28	3707	V	16/07/2009	23/04/2010	24	1.06	Absent	Absent	39	3.6
154	Meena	22	3473	III	30/06/2009	07/04/2010	26	1.35	Absent	Absent	39	2.5
155	Mary	25	4790	V	10/08/2009	17/05/2010	20	0.58	Absent	Absent	39	2.4
156	Ponnamma	26	3421	V	28/06/2009	05/04/2010	26	0.67	Absent	Absent	38	2.7
157	Stella	19	4223	V	02/08/2009	09/05/2010	21	2.31	Present nonsevere	Present Localized	34	2.2
158	Kirthika	28	3889	V	22/07/2009	29/04/2010	22	0.78	Absent	Absent	38	2.9
159	Nayagi	30	3915	IV	22/07/2009	29/04/2010	20	1.02	Present nonsevere	Absent	36	2.45
160	Yamuna	23	3603	III	06/07/2009	13/04/2010	24	1.1	Absent	Absent	39	3.2
161	Neeli	26	3655	V	12/07/2009	19/04/2010	28	1.02	Absent	Absent	37	2.8
162	Roochi	22	3967	V	24/07/2009	01/05/2010	26	3.88	Absent	Present Generalized	34	2.3
163	Parijatham	19	5420	V	01/09/2009	08/06/2010	20	2.65	Absent	Present Localized	38	2.6
164	Punitha	20	5735	V	13/09/2009	20/06/2010	18	1.71	Absent	Present Localized	38	2.8
165	Kala	21	5546	V	07/09/2009	14/06/2010	19	2.28	Absent	Present Localized	39	3.1
166	Arasi	21	4097	V	30/07/2009	06/05/2010	24	1.05	Absent	Absent	38	3.3
167	Vedavalli	26	3681	V	14/07/2009	21/04/2010	26	0.67	Absent	Absent	39	3.5
168	Emolien	20	3291	V	27/06/2009	04/04/2010	28	3.26	Absent	Present Generalized	33	2.2
169	Bavana	19	3759	V	18/07/2009	25/04/2010	20	0.66	Absent	Absent	39	3
170	Kalai	28	3837	V	20/07/2009	27/04/2010	24	0.83	Absent	Absent	38	3.2
171	Sree Priya	29	5672	V	12/09/2009	19/06/2010	22	1.04	Present nonsevere	Absent	37	2.7
172	Neela	28	4071	IV	29/07/2009	05/05/2010	28	0.76	Absent	Absent	38	3.5
173	Kanaga	21	4664	V	09/08/2009	16/05/2010	26	0.57	Absent	Absent	39	3.23
174	Ajanam Beeri	20	5294	V	29/08/2009	05/06/2010	23	2.41	Absent	Present Localized	37	2.7
175	Haseena	19	5798	V	17/09/2009	24/06/2010	20	1.73	Absent	Present Localized	36	2.6
176	Vinodha	21	5483	V	03/09/2009	10/06/2010	22	1.82	Absent	Present Localized	37	2.8
177	Kumari	26	4916	V	18/08/2009	25/05/2010	26	0.67	Absent	Absent	38	3.25
178	Kutti ammal	28	4853	V	15/08/2009	22/05/2010	24	1.03	Absent	Absent	39	2.87
179	Chandra	22	5231	V	27/08/2009	03/06/2010	22	3.91	Absent	Present Generalized	33	2
180	Kanmani	21	5105	V	24/08/2009	31/05/2010	22	0.76	Absent	Absent	37	3.31

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151	Anjali	24	3577	IV	06/07/2009	13/04/2010	26	0.78	Absent	Absent	39	3.1
152	Maaya	26	4160	V	01/08/2009	08/05/2010	22	0.97	Absent	Absent	39	2.9
153	Parvathi	28	3707	V	16/07/2009	23/04/2010	24	1.06	Absent	Absent	39	3.6
154	Meena	22	3473	III	30/06/2009	07/04/2010	26	1.35	Absent	Absent	39	2.5
155	Mary	25	4790	V	10/08/2009	17/05/2010	20	0.58	Absent	Absent	39	2.4
156	Ponnamma	26	3421	V	28/06/2009	05/04/2010	26	0.67	Absent	Absent	38	2.7
157	Stella	19	4223	V	02/08/2009	09/05/2010	21	2.31	Present nonsevere	Present Localized	34	2.2
158	Kirthika	28	3889	V	22/07/2009	29/04/2010	22	0.78	Absent	Absent	38	2.9
159	Nayagi	30	3915	IV	22/07/2009	29/04/2010	20	1.02	Present nonsevere	Absent	36	2.45
160	Yamuna	23	3603	III	06/07/2009	13/04/2010	24	1.1	Absent	Absent	39	3.2
161	Neeli	26	3655	V	12/07/2009	19/04/2010	28	1.02	Absent	Absent	37	2.8
162	Roochi	22	3967	V	24/07/2009	01/05/2010	26	3.88	Absent	Present Generalized	34	2.3
163	Parijatham	19	5420	V	01/09/2009	08/06/2010	20	2.65	Absent	Present Localized	38	2.6
164	Punitha	20	5735	V	13/09/2009	20/06/2010	18	1.71	Absent	Present Localized	38	2.8
165	Kala	21	5546	V	07/09/2009	14/06/2010	19	2.28	Absent	Present Localized	39	3.1
166	Arasi	21	4097	V	30/07/2009	06/05/2010	24	1.05	Absent	Absent	38	3.3
167	Vedavalli	26	3681	V	14/07/2009	21/04/2010	26	0.67	Absent	Absent	39	3.5
168	Emolien	20	3291	V	27/06/2009	04/04/2010	28	3.26	Absent	Present Generalized	33	2.2
169	Bavana	19	3759	V	18/07/2009	25/04/2010	20	0.66	Absent	Absent	39	3
170	Kalai	28	3837	V	20/07/2009	27/04/2010	24	0.83	Absent	Absent	38	3.2
171	Sree Priya	29	5672	V	12/09/2009	19/06/2010	22	1.04	Present nonsevere	Absent	37	2.7
172	Neela	28	4071	IV	29/07/2009	05/05/2010	28	0.76	Absent	Absent	38	3.5
173	Kanaga	21	4664	V	09/08/2009	16/05/2010	26	0.57	Absent	Absent	39	3.23
174	Ajanam Beeri	20	5294	V	29/08/2009	05/06/2010	23	2.41	Absent	Present Localized	37	2.7
175	Haseena	19	5798	V	17/09/2009	24/06/2010	20	1.73	Absent	Present Localized	36	2.6
176	Vinodha	21	5483	V	03/09/2009	10/06/2010	22	1.82	Absent	Present Localized	37	2.8
177	Kumari	26	4916	V	18/08/2009	25/05/2010	26	0.67	Absent	Absent	38	3.25
178	Kutti ammal	28	4853	V	15/08/2009	22/05/2010	24	1.03	Absent	Absent	39	2.87
179	Chandra	22	5231	V	27/08/2009	03/06/2010	22	3.91	Absent	Present Generalized	33	2
180	Kanmani	21	5105	V	24/08/2009	31/05/2010	22	0.76	Absent	Absent	37	3.31

S.No	Name	Age	Register No	Socio Economic class	LMP	EDD	Gestational age at Enrollment (week)	C-Reactive Protein mg/dl	Pre-Eclampsia	Periodontitis	Gestational age at delive	Birth Weight (Kg)
181	Roobini	22	5987	V	03/10/2009	10/07/2010	22	0.55	Absent	Absent	38	3.14
182	Sudha	20	6176	IV	30/10/2009	06/08/2010	18	1.96	Absent	Present Localized	38	2.5
183	Latha	18	5924	V	28/09/2009	05/07/2010	22	1.91	Absent	Present Localized	36	2.4
184	Irfana Begum	22	6050	V	10/10/2009	17/07/2010	20	0.75	Absent	Absent	38	3.22
185	Muniammal	24	5609	V	08/09/2009	15/06/2010	24	0.78	Absent	Absent	39	3.13
186	shajal	20	5357	V	31/08/2009	07/06/2010	25	0.53	Absent	Absent	38	3.15
187	Dhanam	22	4979	V	20/08/2009	27/05/2010	26	4.21	Absent	Present Generalized	35	2.4
188	Gayathri	26	4538	V	06/08/2009	13/05/2010	28	2.22	Absent	Present Localized	37	2.7
189	Murugalakshmi	26	5861	V	17/09/2009	24/06/2010	22	1.01	Absent	Absent	37	3.15
190	Dhatchayani	20	5042	V	23/08/2009	30/05/2010	25	0.55	Absent	Absent	38	3
191	Narmada	28	1861	III	06/05/2009	13/02/2010	27	0.41	Absent	Absent	38	2.86
192	Poorani	26	3239	V	26/06/2009	02/04/2010	20	0.33	Absent	Absent	39	2.9
193	Selvi	19	3525	V	03/07/2009	10/04/2010	19	2.54	Absent	Present Localized	36	2.4
194	Kannagi	30	6113	V	17/10/2009	24/07/2010	20	4.12	Present severe	Present Generalized	32	1.6
195	vasuki	22	2927	V	11/06/2009	18/03/2010	22	0.76	Absent	Absent	37	3.2
196	Kavitha	25	2719	IV	31/05/2009	07/03/2010	28	1.01	Absent	Absent	38	2.9
197	Thangam	22	2251	V	17/05/2009	24/02/2010	26	2.49	Absent	Present Localized	36	2.33
198	Vellaiammal	18	2277	V	17/05/2009	24/02/2010	26	0.62	Absent	Absent	39	3.1
199	Pankajam	19	2667	V	29/05/2009	06/03/2010	24	4.09	Absent	Present Generalized	33	2.4
200	Muthumari	20	3811	IV	19/07/2009	26/04/2010	26	0.43	Absent	Absent	40	3.2

ETHICAL COMMITTEE CERTIFICATE

I, **DR. A. MANGAYARKARASI, M.D(O.G) P.G** apply for the committee certificate for the project

"ASSOCIATION OF MATERNAL PERIODONTAL DISEASE AND RISK OF PRE ECLAMPSIA" under the guidance of **PROF. DR. MEENAUMACHANDER, M.D., D.G.O,** Institute of Social Obstetrics and Govt KGH Chennai.

I understand the implication of doing the research with human subjects and will fully comply with the regulations and keep the dignity and protect the health of subjects at all costs.

Signature of Post graduate student

I have no objection to guide this postgraduate student in the project mentioned above. I shall supervise that all the human rights are protected and research is carried on with the utmost humanitarian principles.

Signature of the guide

Seal of guide

Senior Civil Surgeon
Institute of Social Obstetrics and
Govt. Kasturba Gandhi Hospital for
Women & Children, Chepauk,
Triplicane, Chennai-600 005

I certify that this project has been presented in front of the ethical committee, duly formatted in this institution and that all the members of the Ethical Committee have given permission to conducted this research.

Chairman of Ethical Committee

Date:

CHAIRMAN
ETHICAL COMMITTEE
CHENNAI
Date:-

Seal of Chairman

CHAIRMAN
ETHICAL COMMITTEE
CHENNAI
Date:-

PATIENT CONSENT FORM

STUDY TITLE:

"ASSOCIATION OF MATERNAL PERIODONTITIS AND RISK OF PRE ECLAMPSIA"

STUDY CENTRE:

Institute of Social Obstetrics. Govt.K.G.H. Chennai-5

PARTICIPANT NAME: AGE: SEX: I.D. NO.

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the possible complications that may occur during the procedure. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties of published, unless as required under the law. I agree not to restrict the use of any or results that arise from the study.

I hereby consent to participate in this study of "**ASSOCIATION OF MATERNAL PERIODONTITIS AND RISK OF PRE ECLAMPSIA** "

Signature of Investigator Place:

Date:

Study Investigators Name Institution:

Signature / Thumb impression of patient

Thanking you,

Yours faithfully,

Postgraduate

Guide:

Prof Dr.Meena umachanders,M.D.,D.G.O ,

Institute of social obstetrics&Govt.KGH,

Madras Medical College,

Triplicane, Chennai- 600 005

சுய ஒப்புதல் படிவம்
ஆய்வு செய்யப்படும் தலைப்பு

கர்ப்பிணி பெண்களில் ஈறுநோய் (Periodontitis) மற்றும் உயர் ரத்த அழுத்தத்திற்கும் (Preeclampsia) உள்ள தொடர்பு கண்டறிதல்

ஆய்வு செய்யப்படும் இடம் : சமூக மகப்பேறியில் நிலையம் மற்றும் அரசு கஸ்தூர்பா காந்தி மருத்துவமனை, சென்னை.

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண் :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிகப் பட்டுள்ளது என்பதை அறிந்து கொண்டேன்.	✓
நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என்னை இவ்வாய்வில் இருந்து விலக்கி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	
இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போது இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என் மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிகொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	
இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்கமாட்டேன்.	
இந்த ஆய்வில் நான் பங்குகொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.	

பங்கேற்பவரின் கையொப்பம்..... ....

இடம்:.....தேதி.....கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம் .....இடம் .....தேதி.....

ஆய்வாளரின் பெயர்.....